The Photobromination of β-Styrenesulfonamides and Syntheses of 2-Arylacetylene-1-sulfonamides

Kiyoshi HASEGAWA, Syuzi HIROOKA, Hiroshi KAWAHARA, Atsushi TANAKA, Masahiro NOMURA, and Yutaka HORI

Department of Industrial Chemistry, Faculty of Engineering, Toyama University, Takaoka 933

(Received November 4, 1976)

The photobromination of *trans*-β-styrenesulfonamides in acetic acid at 16—18 °C gave about 75 : 25 mixtures of *threo* (*cis* adducts)- and *erythro*-1,2-dibromo-2-arylethane-1-sulfonamides (*trans* adducts). A similar photobromination of *cis*-β-styrenesulfonamide afforded a 33 : 67 mixture of the *threo* (*trans* adduct)- and the *erythro*-dibromides (*cis* adduct). The diastereomers could be separated by fractional recrystallization. The *cis* adducts were shown to be formed neither by secondary isomerization nor by (presumably) ionic addition. The *trans* dehydrobromination of the *threo*- and the *erythro*-dibromides with Et_3N gave (*Z*)- and (*E*)-β-bromo-β-styrenesulfonamides respectively, which underwent further facile dehydrobromination with aqueous 1 M NaOH at 45—50 °C to afford 2-arylacetylene-1-sulfonamides. They were also prepared from (*Z*)-α-chloro-β-styrenesulfonamide by an analogous procedure.

Triple bonds are more subject to nucleophilic attack than are double bonds.[1] It was, therefore, of interest to synthesize new 2-arylacetylene-1-sulfonic acids and -sulfonyl chlorides and to investigate their reactions with nucleophiles.

Rondestvedt, Jr. previously reported that the sulfonation of phenylacetylene or its acetylide was unsuccessful and the dehydrobromination of β-bromo-β-styrenesulfonic acid and -sulfonyl chloride gave only decomposed products involving no sulfonyl group.[2] He assumed that the *cis* configuration with respect to H and Br atoms makes the dehydrobromination difficult. Since then, acetylenesulfonic acid derivatives have not been studied.

Since an alkali-soluble sulfonamide group would promote dehydrobromination by alkali, we attempted to synthesize 2-arylacetylene-1-sulfonamides (**5**) from β-bromo- (**3**) and α-chloro-β-styrenesulfonamides (**4**). This paper will describe the stereochmistry of 1,2-dibromo-2-arylethane-1-sulfonamides (**2**), **3**, and **4**, and the synthesis of **5** from them.

Results and Discussion

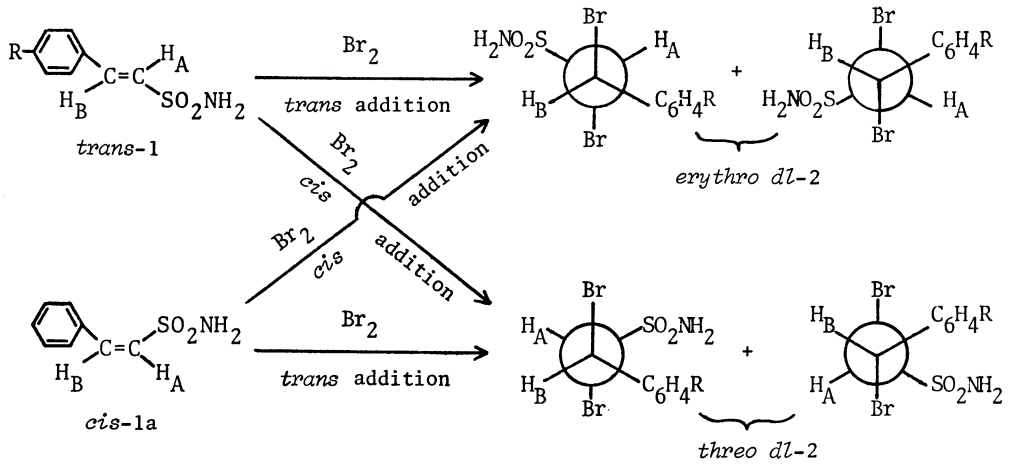
Photobromination of trans- *and* cis-*β-Styrenesulfonamides.* It is known that bromine adds to *trans*-β-styrenesulfonyl chloride in CCl_4[2-4] or to *trans*-β-styrenesulfonamide (*trans*-**1a**, R=H) in acetic acid[2,3] by (presumably) a free-radical mechanism which is catalyzed by light and inhibited by oxygen. However, the stereochemistry of these adducts has not been estabilshed.

According to the procedure of Bordwell *et al.*,[3] *trans*-**1** was photobrominated by sunlight irradiation at 16—18 °C for 30 min. All of the crude products was shown by NMR spectroscopic and high-speed liquid chromatographic analyses to be mixtures of the *threo*- and *erythro*-**2**, predominantly the *threo*. On the contrary, *cis*-β-styrenesulfonamide (*cis*-**1a**) gave a mixture of the diastereomers in which the *erythro* predominated. Table 1 shows the distribution of the diastereomers and their NMR spectroscopic data. The stereochemical relationships are presented in Scheme 1. As the *erythro*-dibromides (R= H, CH_3, and NO_2) are more soluble in benzene than the *threo*, the two isomers could be separated by fractional recrystallization (Table 2). However, the *p*-halogeno-substituted dibromides could not be separated into their diastereomers. The *threo* and *erythro* configurations were assigned to **2** on the basis of the coupling constants (J_{AB}) and the configuration of **3** produced from **2** by *trans* elimination. It is known that the magnitude of the vicinal coupling constant (J_{AB}) depends upon the dihedral angle involved.[5] The diastereomers which have the larger coupling constants were assigned to the *erythro*-**2**, since it seems evident, from a consideration of the steric repulsion by large bromine atoms, that the

Table 1. Addition products of an equimolar amount of bromine to *trans*-**1** and *cis*-**1a** (0.0010 mol) in acetic acid (15 ml) at 16—18 °C for 30 min

R	Yield %	Ratio(%)[a] *threo*	NMR data[b] *threo* H_A	*threo* H_B	*threo* J_{AB}	*erythro* H_A	*erythro* H_B	*erythro* J_{AB}
H[c]	85	74	5.54	5.89	4.0	5.73	5.88	6.5
H[d]	84	33						
CH_3[c]	85	81	5.55	5.88	5.0	5.74	5.86	6.5
Cl[c]	89	76	5.65	5.85	5.0	5.80	5.87	6.5
Br[c]	86	74	5.66	5.84	5.0	5.79	5.88	6.5
NO_2[c]	79	77	5.88	6.01	5.5		e)	

a) Determined by the NMR analysis of the crude products. b) Measured in DMSO-d_6, with TMS as the internal standard; chemical shifts reported in δ(ppm) and coupling constants(J_{AB}) in Hz units. c) *trans*-**1**. d) *cis*-**1a**. e) The chemical shifts are ambiguous.



Scheme 1.

Table 2. *threo-* and *erythro*-dibromides **2**

Compd	R	Mp(°C)	Found(%)				Calcd(%)				IR(KBr)
			C	H	N	S	C	H	N	S	$NH_2(cm^{-1})$
threo-**2a**	H	158—160[a]	28.01	2.80	4.31		28.01	2.64	4.08	9.35	3300, 3400
erythro-**2a**	H	122—123	28.25	2.65	4.02	9.52					3300, 3400
threo-**2b**	CH_3	123—124	30.02	3.12	3.92	8.72	30.27	3.11	3.99	8.97	3260, 3350
erythro-**2b**	CH_3	147—148	30.12	2.91	3.87	8.74					3280, 3390
2c[b]	Cl	142—145	25.71	2.38	3.68	8.60	25.45	2.14	3.71	8.49	3240, 3340 3280, 3400
2d[b]	Br	157—160	22.92	1.96	3.05	7.66	22.77	1.91	3.32	7.60	3240, 3340 3280, 3400
threo-**2e**	NO_2	173—176	24.69	2.07	7.14	8.42	24.76	2.08	7.22	8.26	3240, 3350

a) Lit,[3] mp 161—162 °C. b) They are mixtures of *threo-* and *erythro*-**2**. *threo*(%) : *erythro*(%); (**2c**) = 75 : 25 and (**2d**) = 73 : 27.

conformers shown in Scheme 1 will contribute more heavily to the rotational isomers of the *erythro-* and *threo*-**2**. Figure 1 shows the NMR spectra of *threo-* and *erythro*-**2a** in their methine-field regions. As the AB patterns of both diastereomers could be clearly distinguished, the evaluation of the signal intensities gave an

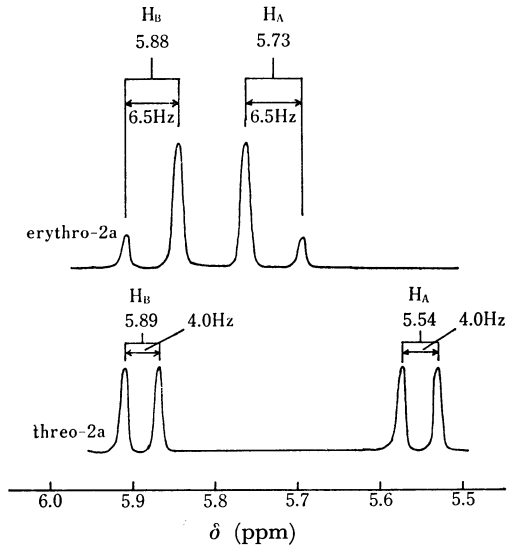


Fig. 1. NMR spectra of *threo-* and *erythro*-**2a** in methine region (DMSO-d_6).

estimate of the amounts of each isomer present. Our conclusion, to be drawn from the subsequent discussion of the configuration of **3**, also supports the stereochemical assignment based upon the coupling constants. The IR spectra of *threo*-**2b**—**e** showed a pair of NH_2 bands at a lower frequency region than the NH_2 bands of the *erythro* isomers.

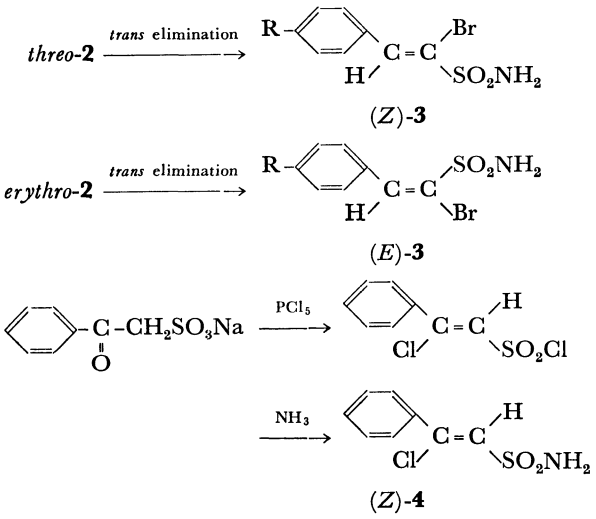
As Bordwell and Rondestvedt, Jr., reported previously,[3] the addition was accelerated by light irradiation. Upon sunlight irradiation at 16—18 °C, the addition was completed within 5 min, but in the dark **2** was prepared in yields of less than 8%. The influence of the reaction time and the temperature on the stereochemistry of the addition was studied in order to find out whether the *cis* adducts were formed in the addition step or whether they arose from the subsequent isomerization of the initially formed *trans* adducts. Under the conditions used, the absence of isomerization between *trans-* and *cis*-**1** prior to the addition was proved by a blank test. The results summarized in Table 3 show that the isomerization of the products is negligible even at high temperatures and that the addition becomes non-stereospecific as the temperature increases. The *cis* addition under sunlight irradiation is a striking feature; however, its explanation must await the results of mechanical studies.

Syntheses of **5** *by Dehydrobromination.* The stereospecific *trans* dehydrobromination of *threo-* and *erythro*-**2**

Table 3. Influence of reaction time and temperature on the distribution of **2**[a]

R	Time (min)	Temp (°C)	Ratio(%) *threo*
H[b]	5	16—18	75
	30	16—18	74
	60	16—18	75
	5	48—50	63
	30	48—50	64
	5	68—70	58
	30	68—70	57
H[c]	5	16—18	33
	30	16—18	33
	5	48—50	49
	5	68—70	54

a) The experiments were carried out under the conditions described in Table 1. b) *trans*-**1a**. c) *cis*-**1a**.



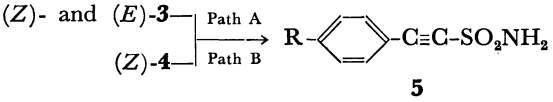
with Et_3N gave *Z* and *E* isomers of **3** respectively. On the other hand, the *Z* isomer of **4** was prepared by the route described below. The results are summarized in Table 4. The *Z* and *E* configurations were assigned to **3** and **4** on the basis of the NMR data and the relative rate measurement of the dehydrobromination from them. The vinyl protons of **3** and **4** resonate about 0.30 ppm upfield from the chemical shifts calculated by the application of the NMR rules[6] of additivity. Since no substituent shielding constants for the SO_2NH_2 group have been reported, the value for the SO_2R group was used. The error must be caused by the shield effect of the NH_2 group. The dehydrobromination experiments of both isomers of **3** in five equiv of aqueous 1 M NaOH at 40 °C for 30 min revealed that not only (*Z*)-**3** is capable of undergoing a facile *β-trans* elimination to

(*Z*)-**3** : δ_{CH}(ppm) = 5.25 + 1.38 + 1.16 + 0.55 = 8.34

(*E*)-**3** : δ_{CH}(ppm) = 5.25 + 1.38 + 0.45 + 0.93 = 8.01

(*Z*)-**4** : δ_{CH}(ppm) = 5.25 + 1.55 + 0.36 + 0.13 = 7.29

give **5**, but, surprisingly, (*E*)-**3** also. The only difference is that the *cis* elimination is slower than the *trans* process. The **5a** sulfonamide was also prepared by the dehydrochlorination of (*Z*)-**4** under the same conditions as held with **3**. The extent of the elimination was measured by the increase in **5** at the expense of **3** and **4** in high-speed liquid chromatography. The configuration and *p*-substituent effects on the elimination are as follows: (*Z*)-**3**; R(reaction %) = NO_2(100) > Cl(23) > Br(22) > H(16) > CH_3(5), (*E*)-**3a**; H(8), and (*Z*)-**4**; H(14). This order is in accord with the idea that electron-attracting groups facilitate elimination reactions.[7] The reason for the greater ease of



5

Table 4. (*Z*)- and (*E*)-monobromides **3** and (*Z*)-monochloride **4**

Compd	R	Mp(°C)	Crystals[a]	NMR in DMSO-d_6 CH(δ)	Found(Calcd), % C	H	N	S	UV $\lambda_{max}^{C_2H_5OH}$ (ε_{max})
(*Z*)-**3a**	H	132—134[b]	needles	8.01	36.38 (36.65)	3.13 (3.08)	5.07 (5.34)	12.26 (12.23)	266 (18500)
(*E*)-**3a**	H	140—142	prisms	7.60	36.50	2.96	5.12	12.32	266 (13400)
(*Z*)-**3b**	CH_3	135—137	plates	8.00	39.23 (39.14)	3.46 (3.65)	4.88 (5.07)	11.93 (11.61)	274 (20600)
(*E*)-**3b**	CH_3	120—122	columns	7.58	38.94	3.49	4.91		276 (14000)
(*Z*)-**3c**[c]	Cl	147—148	plates	8.05	32.69 (32.40)	2.37 (2.38)	4.56 (4.72)	10.91 (10.81)	272 (19500)
(*E*)-**3c**[c]	Cl	133—135	needles	7.60	32.62	2.55	4.62	10.94	272 (14300)
(*Z*)-**3d**[c]	Br	169—171	plates	8.01	28.43 (28.17)	2.16 (2.07)	4.14 (4.11)	9.39 (9.40)	274 (21200)
(*Z*)-**3e**	NO_2	174—176	needles	8.15	31.52 (31.28)	2.28 (2.30)	8.90 (9.12)	10.44 (10.44)	298 (16700)
(*E*)-**3e**	NO_2	159—161	columns	7.58	31.32	2.23	8.88	11.22	294 (14700)
(*Z*)-**4**	H	161—162	needles	7.05	44.36 (44.14)	3.97 (3.70)	6.66 (6.44)	14.64 (14.73)	251 (10300)

a) Recrystallized from benzene. b) Lit,[2] mp 132—133 °C, lit,[3] mp 130—131 °C. c) They were separated by crystal forms.

Table 5. 2-Arylacetylene-1-sulfonamides 5

Compd	R	Yield(%)[a] path A	path B	path C	Mp (°C)	Found(%) C	H	N	S	Calcd(%) C	H	N	S	UV $\lambda_{max}^{C_2H_5OH}$ (ε_{max})
5a	H	72	83	78	136—138	53.16	3.64	7.70	17.47	53.04	3.90	7.73	17.70	248(19800)
5b	CH_3	45		40	149—152	55.16	4.36	7.10		55.37	4.65	7.18		254(21300)
5c	Cl	86		86	162—164	44.37	2.57	6.74	14.90	44.55	2.80	6.50	14.87	256(23500)
5d	Br	84		77	168—169	36.85	2.15	5.13	12.38	36.94	2.33	5.39	12.33	258(26800)
5e	NO_2	76		74	160—161	42.61	2.64	12.44	14.44	42.49	2.67	12.39	14.17	288(17700)

a) Yield after recrystallization from benzene.

the *cis* elimination from (*E*)-**3a** is the previous isomerization to (*Z*)-**3a** and/or the enhanced leaving ability of HBr from such a system when activated by an electron-attracting sulfonyl group.[8] As *cis*-**1a** is known to readily isomerize to *trans*-**1a** upon treatment with aqueous 1 M NaOH,[9] we attempted to detect (*Z*)-**3a** in the reaction mixture of (*E*)-**3a** by high-speed liquid chromatography, but it could not be found. However, this fact does not exclude the idea of the previous isomerization of (*E*)-**3a** if the *trans* elimination proceeds more rapidly than the isomerization.

We concluded that the **3a** sulfonamide (mp 132—133 °C[2] and 130—131 °C[3]), which was previously prepared by the dehydrobromination of the **2a** dibromide (mp 161—162 °C[3]) and by the amidation of β-bromo-β-styrenesulfonyl chloride,[2] has the *Z* configuration, judging from the physical properties and the spectral data.

The **5** sulfonamides were readily synthesized by treating **3** (Path A), (*Z*)-**4** (Path B), or **2** (Path C) with 4—5 equiv of aqueous 1 M NaOH for 5 h at 45—50 °C (Table 5). Both sulfonamides, **2** and **3**, were used without separation into their stereoisomers. The structures of **5** were determined on the basis of the analytical and spectral data. The IR spectrum of **5** displayed a strong absorption band at 2180—2190 cm^{-1} due to the C≡C bond. The **5** sulfonamides are stable enough to be stored for a year.

Experimental

The melting points and the IR, UV, NMR, and mass spectra were measured by the same apparatus as has been reported previously.[9] The high-speed liquid chromatographic analysis was carried out using a JASCO-FLC 150 apparatus on a 0.5 m×2.1 mm column packed with JASCO-DAC SV-O2 (Solvent: methanol (20—40%)-water). The melting points are uncorrected.

cis-*β-Styrenesulfonamide* (cis-***1a***). It was prepared in 100% purity by the method previously described by us.[9] Mp 122—122.5 °C (lit,[10] 96—98 °C).

threo- *and* erythro-*1,2-Dibromo-2-arylethane-1-sulfonamides* (threo *and* erythro-***2***). *General Procedure*: To a solution of *trans*-**1** (0.0010 mol) in purified acetic acid (15 ml) we added an equimolar amount of bromine at 16—18 °C, after which the solution was kept in sunlight at 16—18 °C. Acetic acid in aliquots irradiated for, 5, 30, and 60 min was evaporated *in vacuo* below 30 °C to leave a residue, which was solidified by the addition of ice water. Fractional recrystallization succeeded in separating the *threo* and *erythro* isomers except for the *p*-halogeno-substituted ones. The spectral data for *threo*- and *erythro*-**2a**: *threo*-**2a**: IR(KBr); 3400 and 3300 (NH_2), 1360, 1320, 1160, and 1130 (SO_2), 725 and 700 cm^{-1}. NMR (DMSO-d_6) δ: 5.54 (d, 1, H_A), 5.89 (d, 1, H_B), J_{AB}=4.0 Hz, 7.30—7.50 (m, 5, C_6H_5), and 7.50—7.60 (m, 2, NH_2). MS *m/e*: 343 (M^+). *erythro*-**2a**: IR(KBr); 3400 and 3300 (NH_2), 1350, 1160, and 1145 (SO_2) and 710 cm^{-1}. NMR (DMSO-d_6) δ: 5.73 (d, 1, H_A), 5.88 (d, 1, H_B), J_{AB}=6.5 Hz, 7.30—7.50 (m, 5, C_6H_5), and 7.50—7.60 (m, 2, NH_2). MS *m/e*: 343 (M^+).

(Z,E)-*β-Bromo-β-styrenesulfonamides* ((Z)-***3***, (E)-***3***). *General Procedure*: To a solution of *threo*-**2** (0.00050 mol) in benzene (100 ml) we added Et_3N (0.0020 mol), after which the solution was stirred for 1 h at room temperature. Triethylammonium bromide, which was immediately precipitated, was filtered out, and the filtrate was evaporated to dryness *in vacuo* to leave (*Z*)-**3**. The yields were more than 80%.

Isomers, (*E*)-**3**, were prepared from *erythro*-**2** by using the technique described in the synthesis of (*Z*)-**3**. The spectral data for (*Z*)- and (*E*)-**3a**: (*Z*)-**3a**: IR(KBr); 3350 and 3240 (NH_2), 1330 and 1160 (SO_2) cm^{-1}. NMR(DMSO-d_6) δ; 7.40—7.68 (m, 5, C_6H_5), 7.76—7.86 (m, 2, NH_2), and 8.01 (s, 1, CH). MS *m/e*; 262 (M^+). (*E*)-**3a**: IR(KBr); 3350 and 3240 (NH_2), 1330, 1170, 1160, and 1150 (SO_2) cm^{-1}. NMR(DMSO-d_6) δ; 7.28—7.48 (m, 5, C_6H_5), 7.60 (s, 1, CH), and 7.68 (s, 2, NH_2). MS *m/e*; 262 (M^+).

The dehydrobromination of **2c** (*threo* 75%) and **2d** (*threo* 73%) gave **3c** (*Z* 75%) and **3d** (*Z* 73%) respectively. The (*Z*)- and (*E*)-**3c**, and (*Z*)-**3d** could be separated by crystal forms, but (*E*)-**3d** could not be freed of (*Z*)-**3d**.

(Z)-*α-Chloro-β-styrenesulfonamide* ((Z)-***4***). Sodium benzoylmethanesulfonate (5.0 g, 0.023 mol) was refluxed with PCl_5 (18.7 g, 0.090 mol) for 10 h. The product was worked up in a way analogous to that reported in the synthesis of β-styrenesulfonyl chloride[11] and distilled under reduced pressure to give α-chloro-β-styrenesulfonyl chloride; bp 60—110 °C/3 mmHg (58% yield). Without further purification, it was converted to (*Z*)-**4** by treatment with a 28% ammonia solution. The *E* isomer could not be detected.

2-Arylacetylene-1-sulfonamides (***5***). *Paths A and C*: *General Procedure*: A solution of **3** (Path A) or **2** (Path C) in aqueous 1 M NaOH (50 ml, 0.050 mol) was stirred for 5 h at 45—50 °C and then acidified with concd HCl under cooling to give **5**. Recrystallization from benzene afforded thin plates.

Path B: Sulfonamide **5a** was prepared from (*Z*)-**4** and 1 M NaOH by using the procedure described for Paths A and C.

The spectral data for **5a**: IR(KBr); 3320 and 3210 (NH_2), 2180 (C≡C), 1330, 1180, and 1150 (SO_2) cm^{-1}. NMR (DMSO-d_6) δ; 7.55—7.60 (m, 5, C_6H_5) and 8.24 (s, 2, NH_2). MS *m/e*; 181 (M^+).

References

1) J. March, "Advanced Organic Chemistry, Reactions, Mechanism, and Structure," McGraw-Hill, International Student Ed., Tokyo (1968), p. 575 and cited references.
2) C. S. Rondestvedt, Jr., *J. Am. Chem. Soc.*, **76**, 1926 (1954).
3) F. G. Bordwell and C. S. Rondestvedt, Jr., *J. Am. Chem. Soc.*, **70**, 2429 (1948).
4) C. S. Rondestvedt Jr., R. L. Grimsley, and C. D. Ver Nooy, *J. Org. Chem.*, **21**, 206 (1956).
5) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd ed, Pergamon Press, Germany (1969), p. 291.
6) a) C. Pascual, J. Meier, and W. Simon, *Helv. Chim. Acta*, **49**, 164 (1966); b) S. W. Tobey, *J. Org. Chem.*, **34**, 1281 (1969).
7) Abdel-Hamid A. Youssef and Hamdy M. Abdel-Maksoud, *J. Org. Chem.*, **40**, 3227 (1975).
8) a) Y. Amiel, *J. Org. Chem.*, **39**, 3867 (1974); b) F. G. Bordwell, J. Weinstock, and T. F. Sullivan, *J. Am. Chem. Soc.*, **93**, 4728 (1971).
9) K. Hasegawa, S. Hirooka, T. Sasaki, S. Ikeda, and K. Hashimoto, *Nippon Kagaku Kaishi*, **1975**, 1028.
10) A. P. Terentév, R. A. Gracheva, and Z. F. Shcherbatova, *Chem. Abstr.*, **47**, 3262e (1953).
11) C. S. Rondestvedt, Jr., and F. G. Bordwell, *Org. Synth.*, Coll. Vol. IV, 846 (1963).