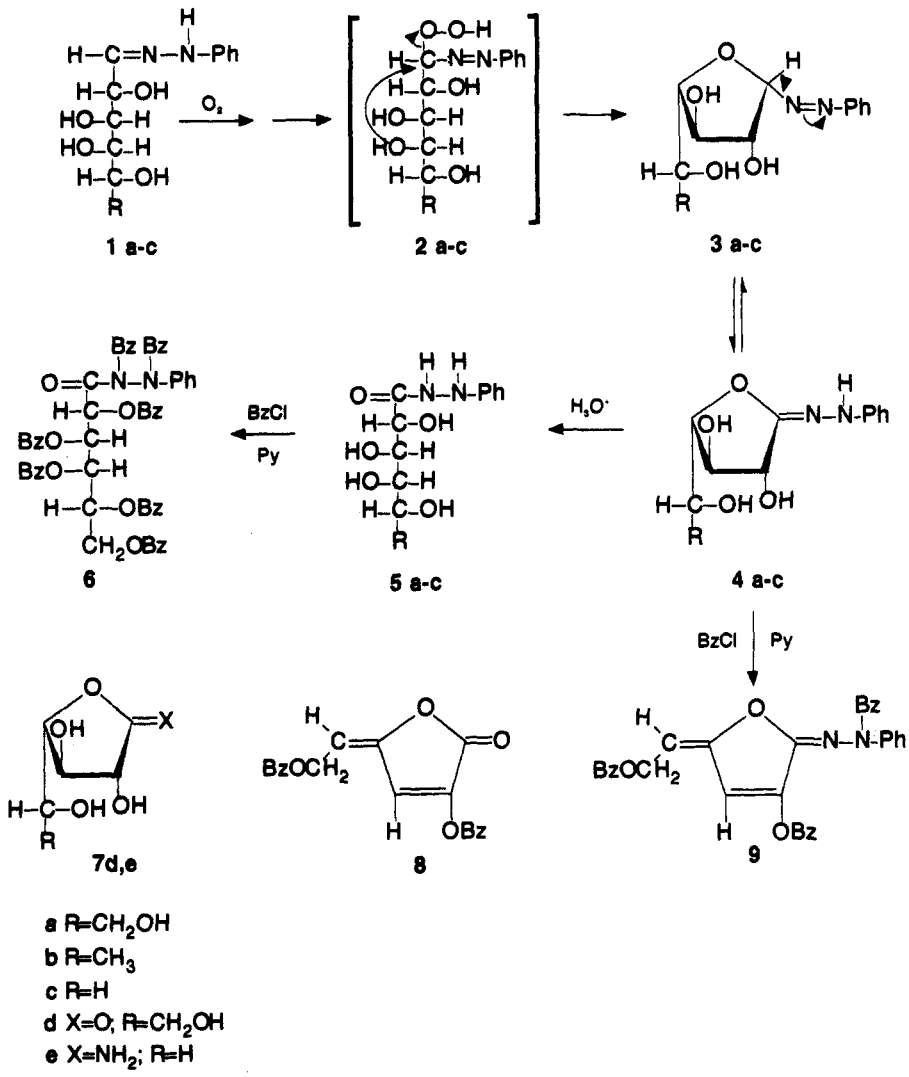
Scheme I



3.73 (m, 1 H, H-5), 3.61 (m, 1 H, H-5'); ^{13}C NMR data (Me_2SO-d_6) δ 150.6 (CN), aromatic 146.4 (C-1'), 129.2 (C-2'), 118.1 (C-3'), 112.4 (C-4'), 86.3 (C-4), 74.8 (C-3), 74.3 (C-2), 60.8 (C-5). Anal. Calcd for $C_{11}H_{14}N_2O_4 \cdot H_2O$: C, 51.56; H, 6.29; N, 10.93. Found: C, 51.40; H, 6.54; N, 10.71.

Hydrolysis of Hydrazono-1,4-lactones 4a-c to Aldonic Phenylhydrazides (5a-c). Suspensions of aldonohydrazono-1,4-lactones **4a-c** and their enantiomers (1.0 g) in water (50.0 mL) containing a drop of concentrated HCl were warmed to 70 °C for 5 h and concentrated to a volume of 5 mL. The products that separated were recrystallized from 95% EtOH in needles, mp 203 °C for **5a**, 108 °C for **5b**, and 215 °C for **5c** and their enantiomers, alone or mixed with authentic samples of the corresponding aldonic phenylhydrazides. HPLC of the mother liquor revealed one product (**5a**, **5b** and **5c** or their enantiomers) and the absence of any epimer.

***N*-Benzoyl-*N*-phenyl-2,6-di-*O*-benzoyl-3,5-dideoxy-2,4-dienoaldohexohydrazono-1,4-lactone (9).** To a cold suspension of *N*-phenyl-D-galactonohydrazono-1,4-lactone (**4a**; 2.0 g) in pyridine (20.0 mL) was added dropwise ice-cold benzoyl chloride (6.0 mL) and kept at room temperature overnight. The brown solution was poured on ice, taken in ether, and washed successively with saturated $NaHCO_3$, 1 M HCl, and water. The residue was triturated with ether and the product (0.4 g) recrystallized from 95% EtOH, in needles, mp 143-144 °C *m/z* 544 (M^+). ^1H NMR data (Me_2SO-d_6): δ 8.02-7.30 (m, 20 H), 7.20 (s, 1 H, H-3), 5.40 (t, 1 H, *J* = 7.61 Hz, H-5), 4.57 (d, 2 H, *J* = 7.63 Hz, H6, 6'). Anal. Calcd for $C_{23}H_{24}N_2O_6$: C, 72.79; H, 4.44; N, 5.14. Found: C, 72.65; H, 4.35; N, 4.99.

***N*,*N'*-Dibenzoylpenta-*O*-benzoyl-D-galactonic Phenylhydrazide (6d).** To a cold solution of D-galactonic phenylhydrazide (**5a**; 3.0 g) in pyridine (60.0 mL) was added ice-cold benzoyl chloride (20.0 mL). After standing overnight at room temperature, the solution was poured onto ice and the oil that separated treated with 95% EtOH. The benzoate (2.0 g) crystallized from 95% EtOH in needles, mp 151-152 °C; ν (KBr) 1726 (O=CO), 1658 (O=CN), 1601 (C=C). Anal. Calcd for $C_{61}H_{46}N_2H_{13}$: C, 72.18; H, 4.57; N, 2.76. Found: C, 72.26; H, 4.65; N, 2.69.

Registry No. D-**1a**, 18841-76-4; L-**1a**, 136981-92-5; D-**1b**, 6035-58-1; L-**1b**, 6055-85-2; D-**1c**, 28767-74-0; L-**1c**, 622-12-8; D-**4a**, 136863-60-0; L-**4a**, 136863-66-6; D-**4b**, 136863-61-1; L-**4b**, 136863-67-7; D-**4c**, 136863-62-2; L-**4c**, 51532-88-8; D-**5a**, 29617-77-4; L-**5a**, 136981-91-4; D-**5b**, 136863-63-3; L-**5b**, 136863-68-8; D-**5c**, 66663-89-6; L-**5c**, 5346-84-9; **6d**, 136863-64-4; **9**, 136863-65-5.

High-Pressure Induced 1,3-Dipolar Cycloadditions of Azides with Electron-Deficient Olefins

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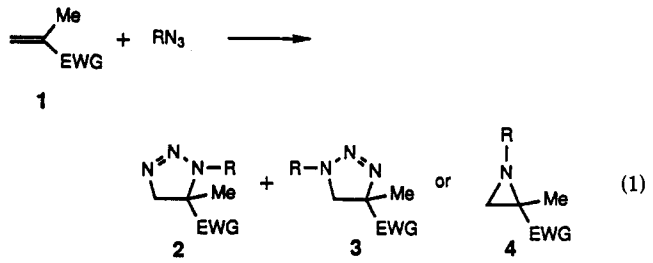
1,3-Dipolar cycloadditions of aryl and alkyl azides with a variety of olefins have been studied in some detail.[1] The

Table I

	high-pressure promoted cycloadditions of methacrylates 1 with azides (12 kbar/24 h)				cycloadditions of methacrylates with azides at 1 atm[3]		
EWG in 1	R	solvent	yield (%)	ratio (3 or 4:2)[a]	time[b] (days)	conversion (%)	ratio (3 or 4:2)
CN	Ph[c]	CH_2Cl_2	79	86:14	30	10	86:14
CO_2Me	Ph	ether	89	68:32	69		75:25
COMe	Ph	ether	93	55:45	20	65	70:30
$CONH_2$	Ph	MeOH	55	>99:1	150	35	90:10
CN	nBu	CH_2Cl_2	72	>99:1	30	25	94:6
CO_2Me	nBu	CH_2Cl_2	86	>99:1	15	65[d]	94:6
COMe	nBu	ether	95	82:18	20	70	92:8
$CONH_2$	nBu	MeOH	64	99:1	150	55	100:0
CN	$PhCH_2$	EtOAc	63	>99:1			
CO_2Me	$PhCH_2$	ether	95	92:8			
COMe	$PhCH_2$	EtOAc	96	80:20			
$CONH_2$	$PhCH_2$	MeOH	67	>99:1			

[a] Ratio determined by ^1H NMR integration. [b] Reactions were run neat. [c] With phenyl azide, triazolines 3 are the predominant products upon depressurization of the reaction mixtures. However, triazolines 3 immediately begin to evolve N_2 and after about 1 week at room temperature only the aziridines 4 are present. [d] Methyl azide was used.

poineering studies of Huisgen[2] and L'abbe[3] established that azide cycloadditions with acrylates and related electron-deficient olefins are generally stereo- and regioselective, but these reactions tend to be very sluggish. For example, methacrylate derivatives 1 cycloadd to afford predominantly regioisomeric triazolines 3 (which sometimes spontaneously decompose to aziridines 4) and smaller amounts of isomers 2 (eq 1). As can be seen from



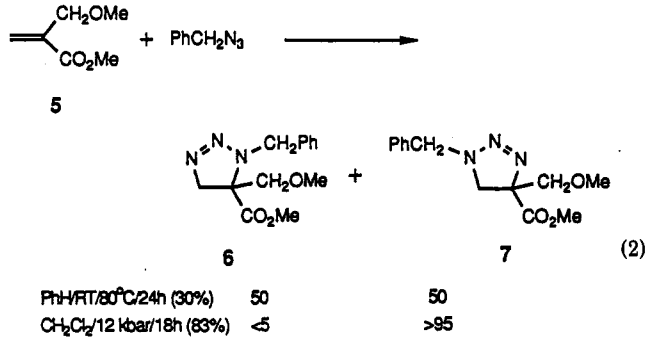
(1)

the work of L'abbe briefly summarized in Table I, these reactions take weeks, or even months, at room temperature to go to only partial completion.[3] Heating is usually precluded in these cycloadditions due to triazoline instability.

In connection with a project in alkaloid synthesis,[4] we required an aziridine of type 4 and therefore became interested in improving the transformation in eq 1. High pressure[5] has proven effective in 1,3-dipolar cycloadditions of nitrones,[6] nitronates,[7] and diazomethane.[8] Moreover, Dauben has reported that electron-deficient arylsulfonyl azides react with electron-rich silylenol ethers at 15 kbar.[9] It seemed reasonable, therefore, that the cycloaddition of azides with electron-deficient alkenes should also be accelerated by pressure.

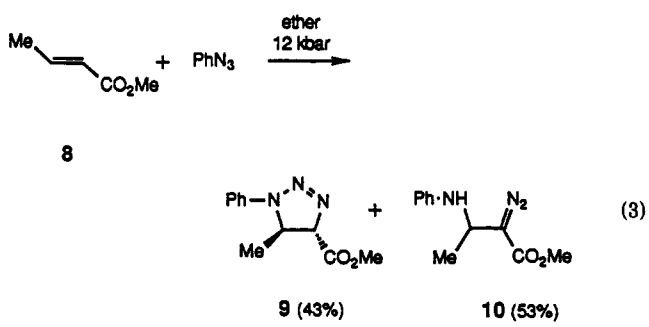
In fact, we have found that methacrylates cycloadd to alkyl and phenyl azides rapidly in generally good yields at 12 kbar at room temperature. The results are listed in Table I. Several different solvents can be used in the high-pressure reactions. However, no systematic survey was done to optimize yields for various substrates with regard to solvent. As can be seen by comparison with the data for the same cycloadditions run at one atmosphere,[3] rate accelerations are significant. Some small variations were observed in the ratios of regioisomeric cycloadducts in the low- vs high-pressure reactions which might be due to solvent differences and/or triazoline decomposition over the long reaction periods at 1 atm.

The more functionalized methacrylate derivative 5 has also been examined (eq 2). We have found that at one atmosphere the cycloaddition of 5 with benzyl azide in refluxing benzene afforded a 1:1 mixture of regioisomeric triazolines 6 and 7 in poor yield. However, at 12 kbar isomer 7 was produced with greater than 95% selectivity in good yield.



(2)

Methyl crotonate (8) and phenyl azide cycloadded at 12 kbar to yield triazoline 9 (43% yield) and the isomeric α-amino diazoester 10 (53% yield) (eq 3). By comparison,



(3)

Huisgen[2] reported that ethyl crotonate and phenyl azide

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(5) For reviews of high-pressure organic reactions see: Asano, T.; LeNoble, W. J. *Chem. Rev.* **1978**, *78*, 407. Matsumoto, K.; Uchida, T. *Synthesis* **1985**, 1. Matsumoto, K.; Sera, A. *Synthesis* **1985**, 999. Matsumoto, K., Acheson, R. M., Eds. *Organic Synthesis at High Pressures*; Wiley: New York, 1991.
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after 14 mos neat at ambient temperature afforded an unspecified yield of an impure amino diazo compound corresponding to **10**, along with a small amount of a 2:1 adduct. None of the triazoline was found.

Thus, azide-electron-deficient olefin dipolar cycloadditions, like many other pericyclic reactions,[5-9] are significantly accelerated by pressure. In view of the increasing availability of preparative high-pressure equipment, this methodology should prove to be synthetically useful in formation of various triazolines and aziridines in a reasonable time scale.

Experimental Section

General Procedure for High-Pressure Cycloadditions. A solution of 2.4 mmol of the azide and 2.7 mmol of the olefin in 1.1 mL of solvent was sealed in a 5-mL plastic Luerlok syringe and subjected to 12 kbar of pressure for 24 h at ambient temperature in a LECO Model PG-200-HPC apparatus.[10] The solvent was removed in vacuo, and the residue was purified by flash chromatography on silica gel eluting with ethyl acetate/hexanes (1:2), except for the methacrylamide products where pure ethyl acetate was used. Data for new compounds are listed below:

Triazoline **3** (EWG = CN, R = CH_2Ph): colorless oil; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.33 (m, 5 H), 4.84 (d, 1 H, J = 15.1 Hz), 4.77 (d, 1 H, J = 15.1 Hz), 3.36 (d, 1 H, J = 10.4 Hz), 2.97 (d, 1 H, $_J$ = 10.4 Hz), 1.59 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 134.2, 128.8, 128.6, 128.4, 128.2, 128.1, 118.6, 71.4, 54.6, 53.9, 22.6; IR (neat) 2235 cm^{-1}.

Triazoline **3** (EWG = CO_2Me, R = CH_2Ph): pale yellow oil; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.34 (m, 5 H), 4.91 (d, 1 H, J = 14.9 Hz), 4.72 (d, 1 H, J = 14.9 Hz), 3.77 (s, 3 H), 3.41 (d, 1 H, J = 10.0 Hz), 2.85 (d, 1 H, J = 10.0 Hz), 1.47 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 171.3, 135.4, 128.7, 128.4, 128.2, 128.1, 127.9, 83.7, 54.2, 53.3, 52.8, 21.8; IR (neat) 1735 cm^{-1}.

Triazoline **3** (EWG = COMe, R = CH_2Ph): pale yellow oil; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.25 (m, 5 H), 4.77 (d, 1 H, J = 14.8 Hz), 4.66 (d, 1 H, J = 14.8 Hz), 3.36 (d, 1 H, J = 10.1 Hz), 2.63 (d, 1 H, J = 10.1 Hz), 2.24 (s, 3 H), 1.34 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 205.3, 135.2, 128.5, 128.0, 127.7, 127.5, 126.8, 89.7, 54.0, 51.1, 25.6, 21.5; IR (neat) 1715 cm^{-1}.

Triazoline **3** (EWG = $CONH_2$, R = CH_2Ph): mp 114-115 °C; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.30 (m, 5 H), 6.76 (bs, 1 H), 6.71 (bs, 1 H), 4.84 (d, 1 H, J = 14.8 Hz), 4.67 (d, 1 H, J = 14.8 Hz), 3.33 (d, 1 H, J = 10.3 Hz), 2.87 (d, 1 H, J = 10.3 Hz), 1.45 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 175.4, 135.3, 128.8, 128.3, 128.2, 128.1, 128.0, 83.8, 54.3, 53.3, 23.3; IR (KBr) 3385, 3190, 1660 cm^{-1}.

Triazoline **6**: pale yellow oil; ^1H NMR $CDCl_3$, 360 (MHz) δ 7.34 (m, 5 H), 4.95 (d, 1 H, J = 15.1 Hz), 4.80 (d, 1 H, J = 15.1 Hz), 3.95 (d, 1 H, J = 10.0 Hz), 3.80 (s, 3 H), 3.75 (d, 1 H, J = 9.9 Hz), 3.57 (d, 1 H, J = 10.4 Hz), 3.25 (s, 3 H), 3.22 (d, 1 H, J = 10.4 Hz); ^{13}C NMR ($CDCl_3$) δ 169.2, 135.2, 128.8, 128.7, 128.3, 128.2, 128.1, 87.6, 68.1, 55.4, 54.1, 53.1, 48.8; IR (neat) 1735 cm^{-1}.

Triazoline **7**: pale yellow oil; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.34 (m, 5 H), 4.90 (d, 1 H, J = 15.0 Hz), 4.83 (d, 1 H, J = 15.0 Hz), 3.81 (d, 1 H, J = 9.7 Hz), 3.79 (s, 3 H), 3.60 (d, 1 H, J = 9.7 Hz), 3.55 (d, 1 H, J = 10.4 Hz), 3.32 (s, 3 H), 3.23 (d, 1 H, J = 10.4 Hz); ^{13}C NMR ($CDCl_3$) δ 169.3, 135.2, 128.8, 128.7, 128.3, 128.2, 128.1, 87.8, 72.9, 59.5, 54.1, 53.1, 48.7; IR (neat) 1735 cm^{-1}.

Triazoline **9**: pale yellow oil; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.32 (m, 5 H), 4.84 (d, 1 H, J = 7.4 Hz), 4.47 (m, 1 H), 3.77 (s, 3 H), 1.29 (d, 3 H, J = 6.3 Hz).

Acknowledgment. We are grateful to the National Institutes of Health (GM-32299) for financial support of this work and thank Professor R. L. Funk for use of the high-pressure apparatus

Registry No. 1 (EWG = CN), 126-98-7; 1 (EWG = CO_2Me), 80-62-6; 1 (EWG = COMe), 814-78-8; 1 (EWG = $CONH_2$), 79-39-0; **2** (EWG = CN, R = Ph), 33708-57-5; **2** (EWG = CO_2Me, R = Ph), 4916-08-9; **2** (EWG = COMe, R = Ph), 33523-93-2; **2** (EWG = COMe, R = nBu), 33549-52-9; **2** (EWG = CO_2Me, R = $PhCH_2$), 136328-08-0; **2** (EWG = COMe, R = $PhCH_2$), 136328-09-1; **3** (EWG = CO_2Me, R = Ph), 136328-10-4; **3** (EWG = COMe, R = Ph), 136328-11-5; **3** (EWG = $CONH_2$, R = Ph), 136328-12-6; **3** (EWG = CN, R = nBu), 136328-13-7; **3** (EWG = CO_2Me, R = nBu), 136328-14-8; **3** (EWG = COMe, R = nBu), 33523-91-0; **3** (EWG = $CONH_2$, R = nBu), 136328-15-9; **3** (EWG = CN, R = $PhCH_2$), 136328-16-0; **3** (EWG = CO_2Me, R = $PhCH_2$), 136328-17-1; **3** (EWG = COMe, R = $PrCH_2$), 136328-18-2; **3** (EWG = $CONH_2$, R = $PhCH_2$), 136328-19-3; **3** (EWG = CN, R = Ph), 136328-20-6; **4** (EWG = CN, R = Ph), 33523-81-8; **4** (EWG = CO_2Me, R = Ph), 4916-07-8; **4** (EWG = COMe, R = Ph), 33549-51-8; **4** (EWG = $CONH_2$, R = Ph), 33523-85-2; **4** (EWG = CN, R = nBu), 33523-88-5; **4** (EWG = CO_2Me, R = nBu), 136328-21-7; **4** (EWG = COMe, R = nBu), 33523-87-4; **4** (EWG = $CONH_2$, R = nBu), 136328-22-8; **4** (EWG = CN, R = $PhCH_2$), 35303-38-9; **4** (EWG = CO_2Me, R = $PhCH_2$), 136328-23-9; **4** (EWG = COMe, R = $PhCH_2$), 136328-24-0; **4** (EWG = $CONH_2$, R = $PhCH_2$), 136328-25-1; **5**, 25328-81-8; **6**, 136328-26-2; **7**, 136328-27-3; **8**, 18707-60-3; **9**, 136328-28-4; **10**, 136328-29-5; $nBuN_3$, 7332-00-5; $PhCH_2N_3$, 622-79-7; PhN_3, 622-37-7.

Supplementary Material Available: NMR spectra of new compounds (12 pages). Ordering information is given on any masthead page.

(10) Available from LECO Corporation, Bellefonte, PA.

Formation and Structure of a Spiro Dimer from Methyl 2,3-Bis(chloromethyl)thiophene-5-carboxylate by Treatment with NaI in DMF Solution

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Recently, it was reported that 2,3-dihydro-2,3-dimethylenethiophene, a thiophene quinodimethane analogue, generated from the corresponding 2,3-bis(halomethyl)- or 2-methyl-3-(halomethyl)thiophene affords mainly the corresponding spiro dimer.[1-3] Unfortunately, it was not possible to determine the structure of the spiro dimer by means of its NMR, IR, or UV spectra. Furthermore, the compound is unstable and may be difficult to derivatize. Therefore, we synthesized a stable spiro dimer bearing an ester group and identified the structure by chemical conversions.

Results and Discussion

When methyl 2,3-bis(chloromethyl)thiophene-5-carboxylate (**1**)[4,5] was treated with NaI in DMF at 60 °C for 7 h, a mixture of spiro dimer **2** and cyclooctene derivative **3** was obtained. However, reaction for 24 h afforded **4**, which is an iodinated derivative of **2** as shown in Scheme I.

Since a distinction among the four possible structures for **2** (Chart I) was not possible from the available spectral data, chemical transformations were undertaken.

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