Reactions of Azines. 15. Preparation of Pyrazolo[1,5-*c*][1,3]oxazepin-6-ones

Edward E. Schweizer,* Cao Zhisong, Arnold Rheingold,† and Martha Bruch‡

Department of Chemistry and Biochemistry, University of Delaware, Newark, Delaware 19716

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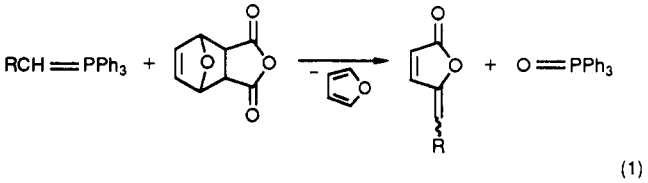
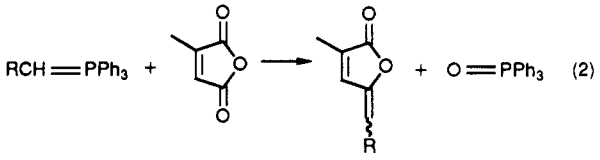
The reactions of azine ylides **1** with isocyanates, ketenes, and other species that contain carbonyl or thiocarbonyl moieties have been shown to provide excellent syntheses of a variety of pyrazolo-fused heterocyclic compounds[1-9] such as pyrazolo[5,1-*c*]oxazines, and 4,9-dihydropyrazolo-[1,5-*b*]isoquinolines,[1,2] 4*H*-pyrazolo[1,5-*c*][1,3,5]oxadiazines,[4] and 4,5-dihydro- and 6,7-dihydropyrazolo[1,5-*a*]-pyridines.[5]

We anticipated on the basis of the previous work that the reactions of azine ylides **1** with maleic anhydride and its mono- or disubstituent derivatives **5** would give the novel pyrazolo[1,5-*c*][1,3]oxazepin-6-one **9** heterocyclic system.

A number of reports in the literature have shown that on reacting stabilized ylides with cyclic anhydrides olefination products occur readily with the ring-closed species being the predominant result.[10-21] However, in the case of the reaction with maleic anhydride the olefination product could not be obtained.[10] The olefination product may be obtained by allowing the ylide to react with the Diels-Alder adduct of maleic anhydride and furan followed by a retro-Diels-Alder reaction[10] (eq 1). The reaction with monomethyl maleic anhydride gave olefination product in low yield[10] (14%) (eq 2).



(1)



(2)

The reaction of azine ylides **1** with anhydrides **5** is depicted in Scheme I. Ylidene **6** is an intermediate product. The final ring-closed product can be obtained by thermal rearrangement of ylidene **6**.

Ylidenes **6a** (R = Me, R^1 = R^2 = H) and **6b** (R = Ph, R^1 = R^2 = H) were obtained as yellow crystalline products by the reactions of azine ylides **1** with the adduct of maleic anhydride **5a** in yields of 52% and 47%, respectively. Ylidene **6m** (R = Ph, R^1 = H, R^2 = Me) was obtained as yellow crystals by the reaction of phosphorane **1** with 2-methylmaleic anhydride in a yield of 12%. The other ylidenes were obtained by the reactions with 2,3-disubstituent maleic anhydrides in good to excellent yields (74% to 90%) as shown in Table I.

All of these intermediate products **6** were obtained as one isomer under the reaction conditions indicated in Table I. In order to show that there could be *E* and *Z* isomers formed in the olefination reaction, the mixture of 2,3-dimethylmaleic anhydride **5** and phosphorane **1** with R = Et in toluene was allowed to react at 80 °C for 15 h. The isomers were found in 75% overall yield with a ratio of 2.4 to 1 for two isomers. The C6-H absorbed at 6.01 ppm for the major isomer and 6.43 ppm for the minor isomer. NOE difference experiments showed a positive NOE between C6-H and the C4-methyl group of the major isomer. No NOE was observed for the minor isomer. Therefore, the major isomer has an *E* configuration, that is, the hydrogen atom on C6 is on same side as the C4-methyl group. The ylidenes **6** have a characteristic absorption around 5.86 ± 0.17 ppm for C6-H (see Table III), thus suggesting that they should be in the *E* form.

The ring-closed products, pyrazolo[1,5-*c*][1,3]oxazepin-

Table I. Preparation of Intermediate 6 and Product 9

product	reactn time (h)	solvent	reactn temp (°C)	mp (°C)[a]	yield (%)[b]
6a	24	toluene	rt[d]	84	52
6b	48	toluene	rt	85	47
6c	15	toluene	reflux	122	85
6d	15	toluene	reflux	144	90
6e	15	xylene	reflux	115	80
6f	15	xylene	reflux	165	84
6g	15	xylene	reflux	194	79
6m	24	toluene	rt	112	12
6o	15	xylene	reflux	134	70
6p	15	xylene	reflux	193	74
9a	48	toluene	reflux	105	100
9b	48	toluene	reflux	183	100
9c	15	xylene	reflux	123	100
9d	15	xylene	reflux	129	100
9e[c]	0.5		200	191	95
9f[c]	0.5		200	184	80
9g[c]	0.5		200	251	85
9h	15	xylene	reflux	121	88
9i	15	xylene	reflux	172	85
9j	15	xylene	reflux	190	87
9k	15	xylene	reflux	148	78
9l	15	xylene	reflux	152	85

[a] Melting points were obtained with a Mel-Temp capillary apparatus and were uncorrected. [b] Yield based on the starting ylide **1**. [c] Reactions were run under vacuum. [d] rt = room temperature.

† For the X-ray data.
‡ For the NOE data.

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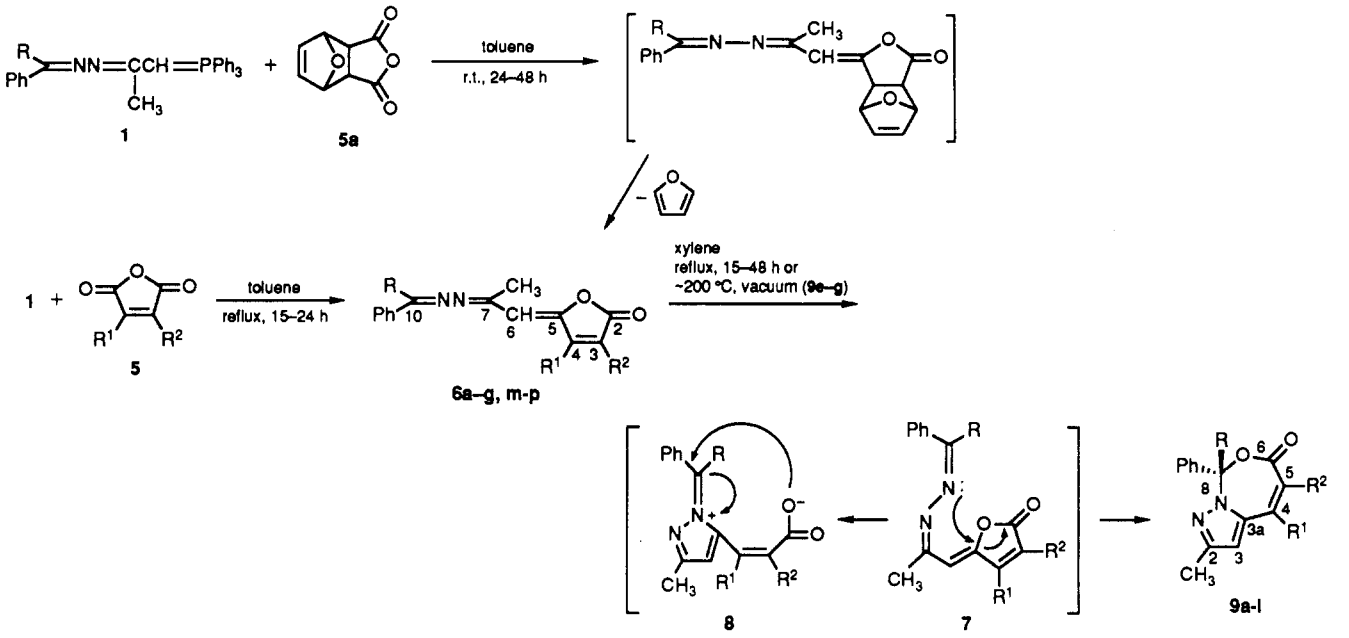
0022-3263/90/1955-6363$02.50/0

Scheme I



1 5a 5 6a–g, m-p 8 7 9a-l

	R	R^1	R^2
6a	Me	H	H
6b	Ph	H	H
6c	Me	Me	Me
6d	Et	Me	Me
6e	Ph	Me	Me
6f	Me	Ph	Ph
6g	Ph	Ph	Ph
6m	Ph	H	Me
6o	PhCO	Me	Me
6p	PhCO	Ph	Ph

	R	R^1	R^2
9a	Me	H	H
9b	Ph	H	H
9c	Me	Me	Me
9d	Et	Me	Me
9e	Ph	Me	Me
9f	Me	Ph	Ph
9g	Ph	Ph	Ph
9h	*n*-Pr	Me	Me
9i	*i*-Pr	Me	Me
9j	Et	Ph	Ph
9k	*n*-Pr	Ph	Ph
9l	*i*-Pr	Ph	Ph

6-ones **9**, were usually obtained by the thermal rearrangement reaction of ylidene **6**. The nature of the substituents R, R^1, and R^2 strongly influenced the reactivity of the thermal rearrangement. Where R was an alkyl group (Me, Et, *n*-Pr, and *i*-Pr) and $R^1 = R^2 = H$ or Me or when R = Ph, $R^1 = R^2 = H$, the rearrangement reaction took place by heating under reflux in xylene. However, when R was phenyl or methyl and $R^1 = R^2 = Ph$ (**6e** and **6f**) or R = Ph and $R^1 = R^2 = Me$ (**6g**), the rearrangement reaction did not take place under refluxing xylene. The products **9e**, **9f**, and **9g** were obtained by heating the corresponding ylidene **6** at 200 ± 10 °C under vacuum. Whereas when R was PhCO (**6o**, **6p**), the rearrangement reaction did not occur.

Examination of the reaction of **6g** (R = Ph, $R^1 = R^2 =$ Ph) by differential scanning callorimetry showed that the ylidene **6g** underwent the rearrangement reaction at 210 °C after melting at 190 °C. The ylidene **6p** (R = PhCO, $R^1 = R^2 =$ Ph) melted at 195 °C and decomposed at 270 °C. Examination of the decomposition mixture by TLC showed at least 7 spots. There was no evidence of the pyrazolooxazepinone **9p** by NMR.

Thus it was shown that the novel pyrazolo[1,5-*c*][1,3]-oxazepin ring system **9** could be produced readily in generally good to excellent yields (Table I).

Spectral Data. The corresponding spectral data are reported in Table II–VI. The numbering scheme is shown in Scheme I. The proton NMR of the final products **9** (Table II) showed characteristic peaks in the range of 2.18–2.41 ppm for C2-methyl protons, and the C3-proton on the pyrazole ring absorbed in the 5.75–6.44 ppm region. The aromatic multiplets fell in the region from 6.43 to 7.47 ppm. The methylene protons, in the ethyl group in **9j** and propyl groups in **9h** and **9k**, are clearly separated due to restricted rotation. In **9j** there were two doublet of quartets at 2.64 and 2.83 ppm, with geminal and vicinal couplings of 14 and 7 Hz, respectively. There were two triple doublets for the α-methylene protons (attached to C8) in **9h** at 2.35 and 2.55 ppm, with couplings of 14, 12, and 4 Hz. Two multiplets are found at 1.36 and 1.55 ppm for the β-methylene protons. For **9k** two triple doublets are found at 2.57 and 2.74 ppm with couplings of 14, 12, and 5 Hz. Two multiplets are found at 1.47–1.60 and 1.65–1.77 ppm.

The proton NMR spectra of **9i** and **9l** showed an unusual pattern for isopropyl protons. The tertiary CH of the isopropyl group showed an unexpectedly broad multiplet. One of the methyl protons in the isopropyl group showed a normal doublet due to the coupling with the adjacent CH, but the other methyl protons in the isopropyl group showed a broad multiplet. The result of an X-ray analysis of **9i** (see Figure 1) gave the distance between N1 and the methyl protons on C16 as 2.44 Å, which is smaller than the van der Waals radii (2.70–2.95 Å for N–H).[22] Therefore, intramolecular interaction restricts the rotation around the C8–C15 bond and C15–C16 bond. The protons on C16 are thus unequivalent. But when the solution temperature of **9i** in $CDCl_3$ was raised to 342 K, the normal doublet was observed, with a *J* value of 6.4 Hz, indicating that the methyl protons on C16 became equivalent due to ready rotation of the isopropyl group.

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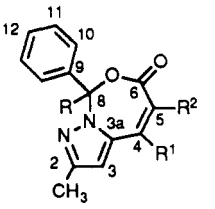
Table II. ^{1}H NMR Spectral Data of Pyrazolo[1,5-*c*][1,3]oxazepin-6-ones 9

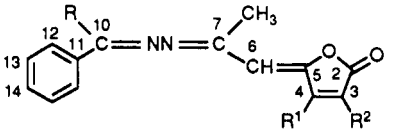


9

compd	R	R^1	R^2	C2-CH_3[a]	C3-H[a]	aromatic	R^2	R^1	R
9a	Me	H	H	2.21	6.34	6.65–6.69 (m, 2 H) 7.18–7.21 (m, 3 H)	5.78 (d, J = 12)	6.60 (d, J = 12)	
9b	Ph	H	Me	2.21	6.44	6.99–7.01 (m, 4 H) 7.32–7.36 (m, 6 H)	5.91 (d, J = 12)	6.79 (d, J = 12)	
9c	Me	Me	Me	2.25	6.30	6.77–6.87 (m, 2 H) 7.25–7.28 (m, 3 H)	1.681 (s) 1.685 (s)	1.834 (s) 1.838 (s)	2.36 (s)
9d	Et	Me	Me	2.36	6.27	6.68–6.84 (m, 2 H) 7.20–7.31 (m, 3 H)	1.71 (s)	1.80 (s)	1.09 (t, 3 H, J = 7, CH_2CH_3), 2.52 (dq, 1 H, J = 7 and 14, $CH_aH_bCH_3$), 2.72 (dq, 1 H, J = 7 and 14, $CH_aH_bCH_3$)
9e	Ph	Me	Me	2.18	6.35	6.99–7.20 (m, 4 H) 7.29–7.33 (m, 6 H)	1.699 (s) 1.703 (s)	1.910 (s) 1.914 (s)	
9f	Me	Ph	Ph	2.32	5.85	6.43–7.38 (m, 15 H)	*b*	*b*	2.37 (s)
9g	Ph	Ph	Ph	2.41	5.88	6.45–7.43 (m, 20 H)	*b*	*b*	
9h	*n*-Pr	Me	Me	2.28	6.20	6.60–6.75 (m, 2 H) 7.15–7.20 (m, 3 H)	1.633 (s) 1.636 (s)	1.716 (s) 1.720 (s)	0.86 (t, 3 H, J = 7, $CH_2CH_2CH_3$), 1.36 (m, 1 H, $CH_2CH_2CH_bCH_3$), 1.55 (m, 1 H, $CH_2CH_aCH_bCH_3$), 2.35 (ddd, 1 H, J = 4, 12, and 14, $CH_aH_bCH_2CH_3$), 2.55 (ddd, 1 H, J = 4, 12, and 14, $CH_aH_bCH_2CH_3$)
9i	*i*-Pr	Me	Me	2.35	6.23	6.60–6.90 (m, 2 H) 7.20–7.30 (m, 3 H)	1.72 (s)	1.76 (s)	0.95 (bm, 3 H, $CHCH_3CH_3$), 1.30 (d, 3 H, J = 7, $CHCH_3CH_3$), 3.11 (bm, 1 H, $CHCH_3CH_3$) $CHCH_3CH_3$), 3.11 (bm, 1 H, $CHCH_3CH_3$)
9j	Et	Ph	Ph	2.31	5.81	6.47–7.44 (m, 15 H)	*b*	*b*	1.16 (t, 3 H, J = 7, CH_2CH_3), 2.64 (dq, 1 H, J = 7 and 14, $CH_aCH_bCH_3$), 2.83 (dq, 1 H, J = 7 and 14, $CH_aCH_bCH_3$)
9k	*n*-Pr	Ph	Ph	2.31	5.80	6.47–7.47 (m, 15 H)	*b*	*b*	0.98 (t, 3 H, J = 7, $CH_2CH_2CH_3$), 1.47–1.60 (m, 1 H, $CH_2CH_aH_bCH_3$), 1.65–1.77 (m, 1 H, $CH_2CH_aH_bCH_3$), 2.57 (ddd, 1 H, J = 5, 12, and 14, $CH_aCH_bCH_2CH_3$), 2.74 (ddd, 1 H, J = 5, 12, and 14, $CH_aCH_bCH_2CH_3$)
9l	*i*-Pr	Ph	Ph	2.30	5.75	6.51–7.41 (m, 15 H)	*b*	*b*	0.91–1.07 (bm, 3 H, $CHCH_{3a}CH_{3b}$), 1.34–1.51 (bm, 3 H, $CHCH_{3a}CH_{3b}$), 3.19–3.27 (bm, 1 H, $CHCH_{3a}CH_{3b}$)

[a] All singlets. [b] With aromatic.

Table III. ^{1}H NMR Spectral Data of Vinylogous Lactone 6



6

compd	R	R^1	R^2	C7-CH_3	C6-H	R	R^1	R^2	aromatic
6a	Me	H	H	2.33	6.31 (dd, J = 0.6, 1.8)	2.18	8.22 (dd, J = 0.6, 5.6)	6.37 (dd; J = 1.8, 5.6)	7.42–7.45 (m, 3 H), 7.88–7.92 (m, 2 H)
6b	Ph	H	H	2.25	6.08 (d, J = 1.7)	*a*	6.00 (dd, J = 5.5, 1.7)	7.12 (d, J = 5.5)	7.18–7.22 (m, 2 H), 7.38–7.45 (m, 6 H), 7.70–7.74 (m, 2 H
6c	Me	Me	Me	2.35	6.01	2.13	2.27	1.98	7.41–7.43 (m, 3 H), 7.87–7.91 (m, 2 H)
6d	Et	Me	Me	2.36	6.01	1.08 (t, J = 7.7) 2.78 (q, J = 7.7)	2.14 2.13	1.97	7.41–7.44 (m, 3 H), 7.86–7.89 (m, 2 H)
6e	Ph	Me	Me	2.46	5.82	*a*	2.03 and 2.02	1.98	7.17–7.22 (m, 2 H), 7.36–7.41 (m, 6 H), 7.66–7.70 (m, 2 H)
6f	Me	Ph	Ph	2.44	6.03	2.22	*a*	*a*	7.18–7.22 (m, 2 H), 7.37–7.41 (m, 6 H), 7.66–7.70 (m, 2 H)
6g	Ph	Ph	Ph	2.54	5.86	*a*	*a*	*a*	7.65–7.68 (m, 2 H)
6m	Ph	H	Me	2.23	5.93	*a*	6.723 and 6.729	1.817 and 1.821	7.21–7.24 (m, 2 H), 7.35–7.47 (m, 6 H), 7.71–7.75 (m, 2 H)
6o	PhCO	Me	Me	2.56	5.69	*a*	1.979 and 1.983	1.93	7.27–7.63 (m, 6 H), 7.78–7.82 (m, 2 H), 7.89–7.93 (m, 2 H)
6p	PhCO	Ph	Ph	2.62	5.70	*a*	*a*	*a*	7.14–7.55 (m, 16 H), 7.76–7.86 (m, 4 H)

[a] With aromatic.

Table IV. ^{13}C **NMR Spectral Data for 5*H*,7*H*-Pyrazolo[1,5-*d*][2,4]oxazepin-8-ones 9**

compd	R	R^1	R^2	C2–CH_3	C2	C3	C3a	C4	C5	C6	C8	C9	C10	C11	C12	R	R^1	R^2
9a	Me	H	H	13.5	148.5	111.7	141.6	128.1	121.4	165.8	93.6	139.0	124.8	128.7	128.8	31.2		
9b	Ph	H	H	13.6	148.4	112.4	139.8	128.5	120.9	165.5	96.3	139.8	127.9	128.1	129.2	*b*		
9c	Me	Me	Me	13.6	147.8	108.6	142.7	142.4	131.4	168.1	92.3	142.4	124.0	128.6	128.3	30.9	19.3	16.9
9d	Et	Me	Me	13.6	147.6	108.4	142.6	141.0	131.3	168.3	94.2	141.0	124.8	128.1	128.1	8.2 (CH_3), 35.4 (CH_2)	19.3	16.9
9e	Ph	Me	Me	13.6	147.4	109.0	140.2	142.8	131.9	167.6	94.2	140.2	127.4	127.9	128.8		19.6	16.8
9f	Me	Ph	Ph	13.5	147.8	112.7	143.1	142.4	133.2	166.5	92.9	142.4[a]	124.9[a]	129.1[a]	128.8[a]	31.3	[a,c]137.0, 127.2, 129.7, 128.8	[a,c]138.3, 127.5, 130.5, 127.8
9g	Ph	Ph	Ph	13.6	147.6	113.3	140.3	142.8	132.9	166.1	95.5	140.3[a]	127.6[a]	128.0[a]	129.2[a]	138.5	[a,c]136.1, 127.1, 129.6, 128.3	[a,c]137.7, 127.8, 130.5, 129.2
9h	*n*-Pr	Me	Me	13.6	147.5	108.4	142.6	141.2	131.3	168.4	94.0	141.2	124.8	128.2	128.2	13.9 ($CH_2CH_2CH_3$), 16.9 ($CH_2CH_2CH_3$), 43.9 ($CH_2CH_2CH_3$)	19.3	16.8
9i	*i*-Pr	Me	Me	13.6	147.2	108.3	143.1	143.1	131.3	168.6	96.2	139.8	125.7	128.2	127.8	17.5, 18.6 [$CH(CH_3)_2$], 36.7 [$CH(CH_3)_2$]	19.3	16.9
9j	Et	Ph	Ph	13.5	147.6	112.5	141.3	142.6	133.5	166.7	94.8	138.3[a]	125.7[a]	129.7[a]	128.7[a]	8.3 (CH_3), 35.7 (CH_2)	[a,c]135.9, 127.1, 128.7, 127.7	[a,c]137.0, 127.5, 130.6, 127.1
9k	*n*-Pr	Ph	Ph	13.1	146.8	111.8	140.7	141.8	132.2	165.9	93.7	137.5[a]	124.8[a]	129.9[a]	128.9[a]	12.7 ($CH_2CH_2CH_3$), 16.1 ($CH_2CH_2CH_3$), 43.4 ($CH_2CH_2CH_3$)	[a,c]135.0, 126.7, 127.9, 126.9	[a,c]136.3, 128.9, 126.3, 127.8
9l	*i*-Pr	Ph	Ph	13.6	147.3	112.6	143.2	140.2	132.9	166.8	96.8	138.5[a]	126.5[a]	130.8	128.6	17.6, 18.3 [$CH(CH_3)_2$], 37.2 [$CH(CH_3)_2$]	[a,c]135.9, 127.1, 129.7, 128.3	[a,c]136.3, 126, 1, 126, 5, 126.6

[a] Assignments uncertain. [b] With C9–C12. [c] Ipso, ortho, meta, para.

Table V. ^{13}C **NMR Spectral Data for Vinylogous Lactone 6**

compd	R	R^1	R^2	C7–CH_3	C2	C3	C4	C5	C6	C7	C10	[a]C11	[a]C12	[a]C13	[a]C14	[a]R	[a]R^1	[a]R^2
6a	Me	H	H	18.5	168.9	122.5	142.2	153.1	113.4	159.0	156.3	137.9	128.4	126.8	130.1	15.3		
6b	Ph	H	H	19.1	169.1	122.0	142.9	153.5	112.2	161.5	157.8	136.7	128.3	129.7	130.4	[b]137.4, 128.3, 129.7, 129.7		
6c	Me	Me	Me	16.6	170.0	125.5	148.3	152.1	108.8	157.4	157.6	138.1	128.4	126.7	129.9	14.8	10.0	8.9
6d	Et	Me	Me	16.7	170.1	125.5	148.4	152.0	108.9	157.3	162.0	136.9	128.5	127.0	129.8	22.0 (CH_2CH_3), 11.6 (CH_2CH_3)	10.1	8.9
6e	Ph	Me	Me	17.2	169.9	125.3	148.3	152.0	108.7	158.4	158.9	135.1	127.9	128.7	129.9	[b]137.9, 129.2, 128.1, 128.9	9.9	8.8
6f	Me	Ph	Ph	16.7	167.9	128.9	151.4	150.3	113.5	157.1	157.5	137.9	128.3	129.1	129.9	14.9	[b]130.0, 128.3, 129.1, 129.7	[b]125.8, 129.2, 128.3, 129.1
6g	Ph	Ph	Ph	17.4	167.9	*c*	151.4	150.4	113.5	158.3	158.0	135.1	127.9	129.1	130.0	[b]138.0, 129.3, 128.2, 128.9	[b]130.0, 128.4, 129.1, 129.7	[b]c, 129.3, 128.8, 129.3
6m	Ph	H	Me	18.9	169.9	128.1	137.2	152.4	109.8	161.5	158.4	136.7	128.1	128.5	130.1	[b]132.6, 128.4, 128.3, 128.1		10.5
6o	PhCO	Me	Me	16.6	169.8	126.0	148.3	153.3	108.5	162.5	163.9	135.1	129.0	128.9	131.3	197.8 (PhCO), [b]133.0, 129.3, 127.7, 134.1	10.0	8.9
6p	PhCO	Ph	Ph	17.0	167.7	*c*	152.5	150.1	112.9	161.7	163.1	135.0	129.0	128.9	131.3	197.3 (PhCO), [b]133.0, 129.3, 127.7, 134.0	[b]129.8, 128.3, 129.1, 129.7	[b]126.7, 129.2, 128.8, 129.0

[a] Aromatic assignments uncertain if many aromatics. [b] Aromatic: ipso, o, m, p. [c] Unable to assign.

Table VI. Mass Spectral Data of Bicyclic Products 9[a,b]

compd	M+	B (M+ - PhCOR)	C (B - CO)	D or E (C - C_3H_4N)
9a	254 (1)	134 (100)	106 (4)	52 (14)
9b	316 (66)	134 (100)	106 (42)	52 (66)
9c	282 (23)	162 (100)	134 (64)	81 (8)
9d	296 (12)	162 (100)	134 (48)	81 (1)
9e	344 (3)	162 (100)	134 (17)	80 (1)
9f	406 (34)	286 (100)	258 (6)	204 (6)
9g	468 (1)	222 (100)	118 (1)	106 (1)
9h	310 (65)	162 (61) 163 (75)	134 (57)	80 (15)
9i	310 (9)	162 (100)	134 (29)	81 (8)
9j	420 (70)	286 (100)	258 (40)	204 (4) 205 (15)
9k	434 (21)	286 (100)	258 (6)	204 (4)
9l	434 (66)	286 (100)	257 (10)	207 (3)

[a] Mass spectra were recorded on a Du Pont 21-492B instrument with a resolution of 3300 or 5000. [b] Relative intensities are in parentheses.

Table VII. Mass Data of Intermediate Products 6[a,b]

product	formula	M+	m/z
6a	$C_{15}H_{14}N_2O_2$	254 (16)	239 (100), 221 (21), 159 (18), 136 (41), 136 (41), 118 (20), 103 (23), 77 (76)
6b	$C_{20}H_{16}N_2O_2$	316 (8)	301 (12), 271 (8), 180 (22), 103 (10), 78 (100), 50 (18)
6c	$C_{17}H_{18}N_2O_2$	282 (61)	267 (100), 223 (52), 149 (22), 118 (63), 103 (34), 77 (81)
6d	$C_{18}H_{20}N_2O_2$	296 (18)	282 (24), 281 (100), 237 (30), 193 (44), 148 (17), 132 (14)8, 77 (40)
6e	$C_{22}H_{20}N_2O_2$	344 (17)	329 (100), 313 (14), 180 (18), 162 (45), 103 (14), 77 (44)
6f	$C_{27}H_{22}N_2O_2$	406 (0.2)	391 (2), 225 (89), 92 (100), 77 (2)
6g	$C_{32}H_{24}N_2O_2$	468 (15)	453 (100), 424 (7), 347 (4), 221 (14), 191 (5), 165 (16), 77 (29)
6m	$C_{21}H_{18}N_2O_2$	330 (21)	315 (68), 283 (29), 238 (30), 196 (80), 149 (70), 77 (31)
6o	$C_{23}H_{20}N_2O_3$	372 (45)	357 (27), 267 (31), 241 (21), 165 (25), 105 (49), 77 (54)
6p	$C_{33}H_{24}N_2O_3$	496 (21)	481 (10), 350 (15), 288 (53), 191 (100), 178 (18), 105 (34), 77 (18)

[a] Mass spectra were recorded on a Du Pont 21-492B instrument with a resolution of 3300 or 5000. [b] Relative intensities are in parentheses.

The proton NMR spectrum at room temperature also showed that the C4-methyl protons and C5-methyl protons in **9c**, **9e**, and **9h** are two pairs of singlets with $CDCl_3$ as solvent. The C4-methyl protons in **9c** are found at 1.681 and 1.685 ppm, the C5-methyl protons at 1.834 and 1.838 ppm. In **9e** C4-methyl protons are found at 1.699 and 1.703 ppm, C5-methyl protons absorbed at 1.910 and 1.914 ppm; in **9h**, 1.633 and 1.636 ppm for C4-methyl protons, 1.716 and 1.720 ppm for C5-methyl protons. Thus, two conformational isomers exist in **9c**, **9e**, and **9h**. At higher temperature, the two singlets collapsed. For example, under room temperature the toluene solution of **9c** absorbed at 1.589, 1.593 ppm for C4-methyl protons and 1.379, 1.383 ppm for C5-methyl protons; when the solution temperature of **9c** was raised to 375 K, only singlets for C4-methyl protons and C5-methyl protons were observed at 1.58 and 1.46 ppm, respectively.

The C4-methyl protons in **6d**, **6e**, **6m**, and **6o** also showed two pairs of singlets with $CDCl_3$ as solvent under room temperature. With toluene-d_8 as solvent, the two singlets collapsed. For example, C4-methyl protons in **6e** are found at 2.03 and 2.02 ppm in $CDCl_3$. With toluene-d_8 as solvent, a singlet for C4-methyl protons is observed at 1.49 ppm.

The mass spectral data of the intermediate products **6** and bicyclic compounds **9** are reported in Table VI and VII. The mass spectral data of bicyclic compounds **9** (Table IV) showed characteristic decomposition patterns. The aromatic ketones (PhCOR) are lost in the first step. In the table fragments B are the basic peaks. The pro-

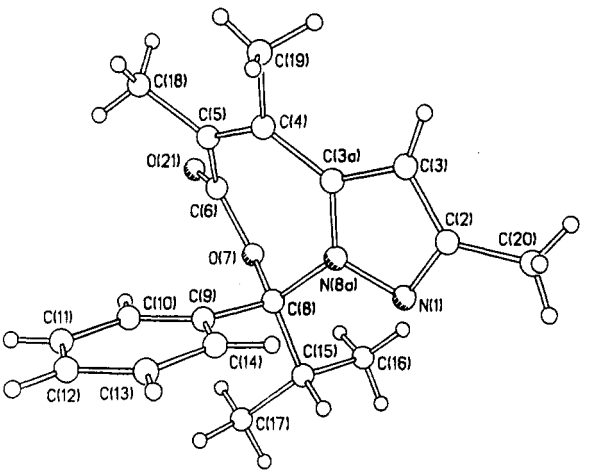
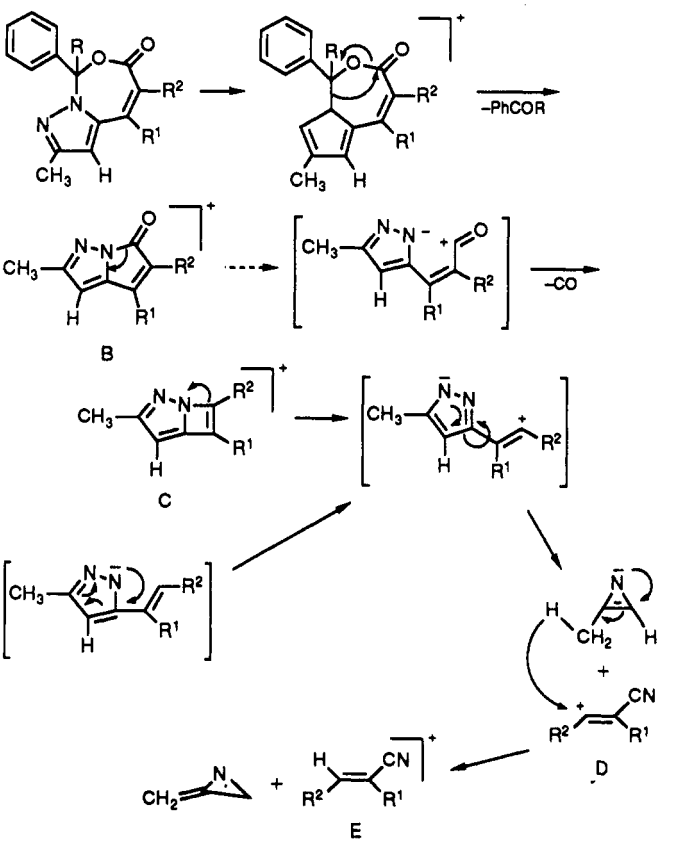


Figure 1. ORTEP diagram of 4,5,8-trimethyl-8-phenylpyrazolo-[1,5-*c*][1,3]oxazepin-6-one (**9i**).

Scheme II



posed decomposition pathway is depicted in Scheme II.

Melting points were obtained on a Mel-Temp capillary apparatus and were uncorrected. The ^1H and ^{13}C NMR spectra of a approximately 10% (w/v) solution in $CDCl_3$ were obtained on a Bruker Spectrospin Model WM 250 or AM 250 or on a Nicolet QE 300 instrument. Precise mass spectra were recorded by using a Du Pont 21-492B instrument with a resolution of 3300 or 5000. Baker silica gel (60-200 mesh) was routinely used throughout for product separation. Eastman Chromagram (silica gel with a fluorescent indicator on polyethylene) precoated sheets were employed in thin-layer chromatographic (TLC) operations.

Preparation of Intermediate Product 6. General Procedure. Purified monosubstituted or disubstituted maleic anhydride **5**, or the Diels-Alder adduct of maleic anhydride and furan **5a** (4 mmol), was added, all at once, to a slurry of phosphorane ylide 1 (3 mmol) in dry toluene (50 mL). The mixture was stirred under room temperature (for **6a,b,m**) or under reflux (for **6c-g,o,p**) for 15 to 24 h. Then the mixture was chromatographically separated with diethyl ether-petroleum ether as eluent (ratio range: 1:9 to 1:4). The crude product was purified by recrystallization from diethyl ether. The pure product **6** was obtained as yellow crystals. TLC showed one spot. The results are reported in Table I.

Preparation of *Z* and *E* Isomers of Ylidene 6d. Sublimed 2,3-dimethylmaleic anhydride **5** (0.4 g, 3.2 mmol) was added, all at once, to a slurry of phosphorane 1 with R = Et (0.8 g, 1.8 mmol) in 30 mL of dry toluene. The mixture was stirred at 80 °C for 15 h. After being cooled down to room temperature, the mixture was chromatographically separated (petroleum ether-diethyl ether, only petroleum ether used at the beginning and 4:1 at the end). The solution was allowed to stand until two isomers of ylidene **6d** crystallized from the eluent. The total yield of the isomers was 75%, and the ratio of *E* form to *Z* form was 2.4:1. ^1H NMR ($CDCl_3$, TMS as internal standard) for the mixture of *Z* and *E* forms: 1.08 (t, J = 7.6 Hz, CH_2CH_3), 1.96 (s, C3-CH_3), 1.98 (s, C3-CH_3), 2.06, 2.05 (ds, C4-CH_3), 2.15, 2.14 (ds, C4-CH_3), 2.36 (s, C7-CH_3), 2.51 (s, C-7CH_3), 2.78, (q, J = 7.6 Hz, CH_2CH_3), 2.86 (q, J = 7.6 Hz, CH_2CH_3), 6.01 (s, C6-H), 6.43 (s, C6-H), 7.42-7.90 (m, all Ar-H for two isomers) ppm.

Thermal Rearrangement of Ylidene 6 into Bicyclic Product 9 in Solution. General Procedure. The pure sample **6** (200 mg) was dissolved in dry xylene (50 mL). The solution was heated under reflux with vigorous stirring for 15 to 48 h. After cooling down to room temperature, the solvent was removed on a rotary evaporator. The residue was dissolved in CH_2Cl_2 (1 mL) and then separated on a chromatographic column with diethyl ether-petroleum ether as eluent (1:4). The pure product recrystallized from diethyl ether was obtained as white crystals. TLC showed one spot. The results are reported in Table I.

Thermal Rearrangement of Ylidene 6e, Neat (6f and 6g). The pure sample (100 mg) was placed in a subliming tube and was heated to 200 °C in a sand bath under vacuum for 0.5 h. After being cooled down to room temperature, the sample was dissolved in CH_2Cl_2 (5 mL). Chromatogrpahy of the solution with diethyl ether-petroleum ether as eluent (1:3) gave the pure product, which was collected and recrystallized from diethyl ether as white crystals. TLC showed one spot. The results are reported in Table I.

Measurement of Rearrangement and Decomposition Temperature for Ylidenes 6h and 6p. The differential thermal analysis was undertaken on a Mettler 200 differential thermal analyzer. The heat capacity of the sample was measured. The scanning was done with about a 2-mg sample in a scaled aluminum pan. The scanning speed was 5° per min. The scanning range was 50 to 300 °C. The instrument was calibrated with benzoic acid and indium metal.

Measurement of NOE Difference for the *E* and *Z* Isomers of Ylidene 6d. NOE difference experiments were obtained on a Bruker AM 250 NMR spectrophotometer. A total of 64 to 128 scans were accumulated for both the on-resonance and off-resonance spectra. The irradiation time was 5 s, the relaxation delay was 2 s, and the acquisition time was 2.3 s for each scan. The decoupler power employed was the minimum power required to completely saturate the C6-H resonance for each isomer without affecting the neighboring resonance.

Crystallographic Structural Determination for 9i. The structure of **9i** was obtained at ambient temperatures (22-24 °C) with a Nicolet R3m diffractometer. All software is contained in the SHELXTL (5.1) software package (G. Sheldrick, Nicolet XRD, Madison, WI). Crystal data for $C_{19}H_{22}N_2O_2$: triclinic, $P\bar{1}$, a = 7.826 (3) Å, b = 9.427 (5) Å, c = 12.183 (6) Å, α = 77.54 (4)°, β = 86.56 (3)°, γ = 72.02 (3)°, V = 834.9 (7) Å^3, Z = 2, μ(Mo Kα) = 0.75 cm^{-1}, D(calcd) = 1.234 g/cm^3. Data were collected (Nicolet R3m, $2\theta_{max}$ = 46°) yielding 1895 independent observed reflections $F_o > 3\sigma(F_o)$. No absorption correction was applied (low μ, well-shaped crystal). All non-hydrogen atoms were refined anisotropically, while all hydrogen atoms were found and refined isotropically. $R(F)$ = 4.48%, $R(wF)$ = 4.87%, GOF = 1.194, $\Delta(\rho)$ = 0.156 e Å^{-3}; Δ/σ = 0.020, and N_o/N_v = 6.4. Tables of atomic coordinates, bond distances and angles, and anisotropic temperature coefficients are available as supplementary material.

Registry No. **1a**, 87101-43-7; **1b**, 87101-42-6; **1d**, 107353-13-9; **1h**, 129467-93-2; **1i**, 125229-36-9; **1o**, 63570-25-2; **5a**, 5426-09-5; **5c**, 766-39-2; **5f**, 4808-48-4; **5m**, 616-02-4; **6a**, 129467-94-3; **6b**, 129467-95-4; **6c**, 129467-94-3; **6d**, 129467-96-5; **6e**, 129467-97-6; **6f**, 129467-98-7; **6g**, 129467-99-8; **6h**, 129468-00-4; **6i**, 129468-01-5; **6j**, 129468-02-6; **6k**, 129468-03-7; **6l**, 129468-04-8; **6m**, 129468-05-9; **6o**, 129468-06-0; **6p**, 129468-07-1; **9a**, 129468-08-2; **9b**, 129468-09-3; **9c**, 129468-10-6; **9d**, 129468-11-7; **9e**, 129468-12-8; **9f**, 129468-13-9; **9g**, 129468-14-0; **9h**, 129468-15-1; **9i**, 129468-16-2; **9j**, 129468-17-3; **9k**, 129468-18-4; **9l**, 129468-19-5.

Supplementary Material Available: Tables of atomic coordinates, isotropic thermal parameters, bond distances and angles, and X-ray crystallographic data for **9i** (7 pages). Ordering information is given on any current masthead page.

Versatile Methods for the Synthesis of Differentially Functionalized Pentaerythritol Amine Derivatives

T. Jeffrey Dunn, William L. Neumann,* Milorad M. Rogic, and Steven R. Woulfe*

Department of Organic Chemistry, Mallinckrodt Medical, Inc., St. Louis, Missouri 63134

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Polyamine systems are important materials for a variety of bioorganic applications ranging from the area of molecular recognition to the coordination of metals in biological systems.[1] The important triamine 1,1,1-tris-

(1) For excellent reviews, see: Lehn, J. M. In *Synthesis of Macrocycles*; Itzatt, R. M., Christensen, J. J., Eds.; Wiley: New York, 1987; Chapter 4. Lehn, J. M. *Angew. Chem., Intl. Ed. Engl.* **1988**, *27*, 89.

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