Communications

1,4-Bridged Pyrazolin-5-ones from Thermal Ring Enlargement of Spiro Pyrazolium Ylides

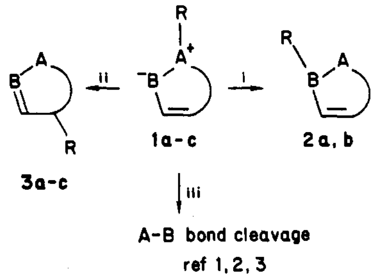
Summary: Spiro pyrazolium ylides **5** obtained by flow pyrolysis of hydrazinopropenoate derivatives **4** undergo a thermally induced ring enlargement by a [1,4] sigmatropic shift leading to 1,4-bridged pyrazolin-5-ones **6**; in some cases a competing reaction is the intramolecular elimination which affords *N*-alkenyl-5-hydroxypyrazoles **7**.

Sir: During the past few years, a few examples of rearrangements of endocyclic unsaturated ylides of type **1** have been reported. The three main pathways postulated to account for the formation of isolated products (Scheme I) can be regarded as (i) the Stevens [1,2] rearrangement,[1] (ii) the [1,4] migration of a substituent R,[2] and (iii) the A–B bond cleavage reaction.[3] Moreover, it has been shown in some cases that two or more of these processes can compete.

We have recently reported[4] the clean thermal rearrangement of pyrazolium ylides **1c** to pyrazolinones **3c**, implying a [1,4] methyl shift from nitrogen to carbon (path ii). We anticipated that this new intramolecular rearrangement which formally involves a 6π electron system might be extended to spiro cyclic derivatives such as **5**. We report here a simple and efficient synthesis of 1,4-bridged pyrazolinones **6**, a new class of diazabicyclo compounds now available from hydrazinopropenoate derivatives **4** (Scheme II).

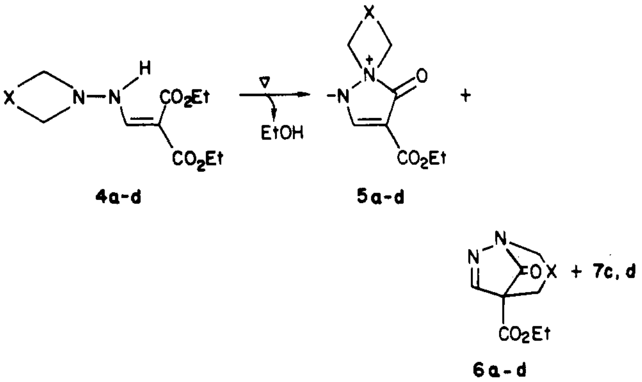
Diesters **4a–d** were obtained in high yields (>95%) by condensation in methanol of the appropriate *N*-amino heterocycle with diethyl ethoxymethylenemalonate.[5] When solutions of compounds **4a–d** in toluene were submitted to flow pyrolysis[6] at relatively low temperatures (325–350 °C), spirocyclic pyrazolium ylides **5a–d**,[7] resulting from successive [1,4] elimination of ethanol and 6 π electrocyclization of the intermediate ketene,[8] were obtained in fair yields (56–74%) after recrystallization. In this temperature range, small amounts of the expected bridged pyrazolinones were formed and could be isolated by flash column chromatography[9] of the mother liquors (see Table I).

Scheme I[a]



[a] a, A = S, B = N (ref 1, 2); b, A = NMe, B = CH (ref 3); c, A = NMe, B = N (ref 4).

Scheme II[a]



[a] a, X = $(CH_2)_2$; b, X = CH_2OCH_2; c, X = $(CH_2)_3$; d, X = $(CH_2)_4$.

Table I. Flow Pyrolysis[a] of Hydrazinopropenoates 4

starting compounds[b]	temp, °C	product distribution, %		
		5[b,c]	6[b]	7
4a	335	63[d]	10	
4a	400	27	47	
4b	360	73	15	
4b	400	16	44[f]	
4c	355	74	20	
4c	400	25	36[f]	16[g]
4c	420		23	38
4d	325	56[e]		
4d	390		48[f]	15[g]

[a] Typical procedure is given in ref 6a. [b] Satisfactory analytical data (±0.2% for C, H, N). [c] mp (°C) of ylides **5** recrystallized from Et_2O: **5a** (90–92), **5b** (138), **5c** (83), **5d** (103). [d] 20% recovered starting material. [e] 15% recovered starting material. [f] mp (°C) of pyrazolinones crystallized from light petroleum: **6b** (62), **6c** (45), **6d** (36). [g] Estimated yield by ^1H NMR of crude products.

In preliminary experiments, we observed the facile intramolecular thermal rearrangement of ylides **5** to bicyclic derivatives **6**. However, for preparative purposes, it was not necessary to isolate intermediate ylides **5** since better overall yields were obtained when starting diesters **4** were directly submitted to thermolysis at higher temperatures.[10] Under these experimental conditions, compounds **4a,b** led

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[1] Grant, R. D.; Moody, C. J.; Rees, C. W.; Tsoi, S. C. *J. Chem. Soc., Chem. Commun.* **1982**, 884.

[2] Hori, M.; Kataoka, T.; Shimizu, H.; Matsuo, K. *Tetrahedron Lett.* **1979**, 3969.

[3] (a) Jacobson, A. E. *J. Org. Chem.* **1966**, *31*, 1569. (b) Jacobson, A. E.; Parfitt, R. T. *J. Org. Chem.* **1967**, *32*, 1894.

[4] Coqueret, X.; Bourelle-Wargnier, F.; Chuche, J.; Toupet, L. *J. Chem. Soc., Chem. Commun.* **1983**, 1144.

[5] Santilli, A. A.; Bruce, W. F.; Osdense, T. S. *J. Med. Chem.* **1964**, 7, 68.

[6] (a) A solution of starting compound 4 (600 mg in 25 mL of toluene) is dropped through a hot vertical Pyrex tube (60 cm in length, 2 cm in diameter, filled with Pyrex balls) under reduced pressure (20 torr). (b) Brown, R. F. C. "Pyrolytic Methods in Organic Chemistry"; Academic Press: New York, 1980; p 23.

[7] For another route to spiro pyrazolium ylides, see: Grohe, K.; Heitzer, H.; Wendisch, D. *Liebigs Ann. Chem.* **1982**, 1602.

[8] Maujean, A.; Marcy, G.; Chuche, J. *Tetrahedron Lett.* **1980**, *21*, 519.

[9] Still, W. C.; Khan, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

[10] Maximum yields of 6 were obtained at about 400 °C. See: Table I.

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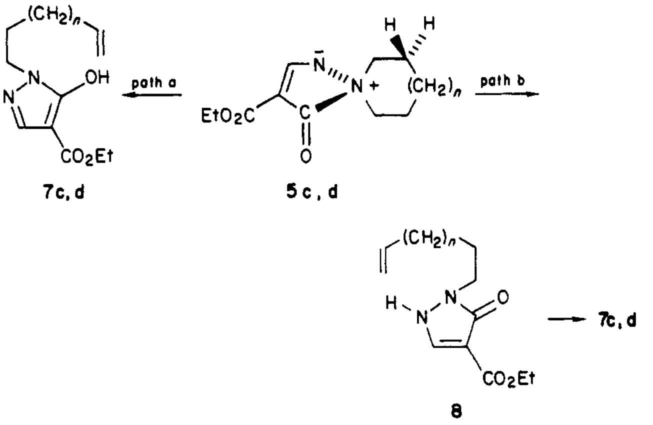
Scheme III[a]



[a] c, $n = 1$; d, $n = 2$.

to pyrazolinones **6a,b** together with ylides **5a,b** as minor products. Bridged 2-pyrazolin-5-ones **6a,b**, whose structures are supported by ^1H and ^{13}C NMR spectroscopy, show two strong infrared absorption bands in the 1700–1800-cm^{-1} range. The first band (1740 cm^{-1}) is assigned to the ester carbonyl while we attribute the second one (1765 cm^{-1} for **6a** and 1760 cm^{-1} for **6b**) to the amide carbonyl. These abnormal high values for an amide band reveal, in accordance with Bredt's rule, an important inhibition of the N—C═O resonance in these N-bridgehead lactams.[11]

On the other hand, ^1H NMR spectra of the crude materials obtained from diesters **4c,d** at 390–400 °C showed the characteristic signals of a terminal vinyl group suggesting that an elimination reaction follows or competes with the [1,4] migration. Flash column chromatography of the mixture resulting from the thermolysis of the piperidine derivative **4c** afforded besides the pyrazolinone **6c**[12] an isomeric *N*-alkenyl compound whose spectroscopic data[13] support the hydroxy-5-pyrazole structure **7c**. The analogous elimination product **7d** formed in lower yield (15% estimation on the basis of ^1H NMR spectra) could not be isolated.

Pyrazolinone **6c** submitted to flow pyrolysis at 400 °C was recovered unchanged. Thus hydroxy-5-pyrazoles **7c,d** result from an intramolecular elimination reaction of ylides **5c,d** (Scheme III), either by a six-center mechanism involving the negative charge delocalized on the carbonyl oxygen (path a) or by a Cope-type elimination[14] (path b) and subsequent isomerization (**8** → **7**) to the stable tautomer in aprotic media.[15] We believe that the elimination takes place according to the latter pathway since crystallographic analyses of analogous ylidic compounds reveal a very short C═O bond distance.[16]

As observed, the limited ring deformations of the five-membered pyrrolidinium ylide **5a** do not permit an intramolecular elimination reaction. The unexpected behavior of the six-membered morpholinium ylide **5b**, unreactive toward elimination in contrast with the isosteric piperidinium derivative **5c**, should be rationalized in terms of stereoelectronic effects which need further investigation.

We have demonstrated that the flow pyrolysis of the readily available hydrazinopropenoates **4** offers a convenient method for the preparation in one experimental step of a new class of diazabicyclo compounds **6**. Studies are now underway toward the extension to other systems of this novel ring enlargement methodology.

Registry No. **4a**, 94621-01-9; **4b**, 94621-02-0; **4c**, 94621-03-1; **4d**, 94621-04-2; **5a**, 94621-05-3; **5b**, 94621-06-4; **5c**, 94621-07-5; **5d**, 94621-08-6; **6a**, 94621-09-7; **6b**, 94621-10-0; **6c**, 94621-11-1; **6d**, 94621-12-2; **7c**, 94621-13-3; **7d**, 94621-14-4; 1-aminopyrrolidine, 16596-41-1; 4-aminomorpholine, 4319-49-7; 1-aminopiperidine, 2213-43-6; 1-aminohexahydro-1*H*-azepine, 5906-35-4; diethyl(ethoxymethylene)malonate, 87-13-8.

Supplementary Material Available: ^1H and ^{13}C NMR spectral data for pyrazolinones **6a–d** (1 page). Ordering information is given on any current masthead page.

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[11] Hall, H. K.; El-Shekeil, A. *Chem. Rev.* **1983**, *83*, 549. Pracejus, H.; Kehlen, M.; Kehlen, K.; Matschiner, H. *Tetrahedron* **1965**, *21*, 2257.

[12] Selected IR data (cm^{-1}): **6c** ($CHCl_3$) ν(COOEt) 1750, ν(NC═O) 1725; **6d** ($CHCl_3$) ν(COOEt) 1750, ν(NC═O) 1715.

[13] Compound **7c**: IR ($CHCl_3$) two strong absorptions at ν 1580 and 1670 cm^{-7}, ^1H NMR ($CDCl_3$-Me_4Si) δ 1.35 (3 H, t, J = 7 Hz), 2.05 (4 H, m), 3.95 (3 H, t, J = 7 Hz), 4.30 (3 H, t, J = 7 Hz), 5.05 (2 H, m), 6.75 (1 H, m), 7.20 (1 H, br s), 7.55 (1 H, s); ^{13}C NMR ($CDCl_3$-Me_4Si) δ 14.4 (q), 27.8 (t), 30.0 (t), 45.1 (t), 58.9 (t), 95.1 (s), 115.4 (t), 137.6 (d), 138.7 (d), 154.0 (s), 162.6 (s).

[14] Bach, R. D.; Andrzejewski, D.; Bair, K. W. *J. Chem. Soc., Chem. Commun.* **1974**, 820. Cope, A. C.; Le Bel, N. A. *J. Am. Chem. Soc.* **1960**, *82*, 4656.

[15] Jensen, B. S. *Acta Chem. Scand.* **1959**, *13*, 1668. For a recent investigation of the tautomerism of pyrazolin-5-ones, see: Gelin, S.; Chantegrel, B.; Nadi, A. I. *J. Org. Chem.* **1983**, *48*, 4078.

[16] The C(5)═O bond distance in 1,1-dimethyl-4-(methoxycarbonyl)-5-oxo-3-pyrazolinium ylide and in 4-cyano-1,1-dimethyl-5-oxo-3-pyrazolinium ylide is found to be 1.198 Å and 1.204 Å, respectively (crystallographic data are available from the Cambridge Crystallographic Data Center, see ref 4). The cyclic carbonyl bond length in ylides **5** which is therefore about 1.20 Å is consistent with a low contribution of the pyrazolium-5-olate resonance structure which would have favored the six-center Hofmann-type elimination mechanism. For a related discussion on C–O bond distance in betaines, see: Neugebauer, F. A.; Fischer, H.; Krieger, C. *Tetrahedron Lett.* **1984**, *25*, 629.

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Allylzinc Reagent Additions in Aqueous Media

Summary: Homoallylic alcohols are obtained when allylic halides, zinc, and aldehydes or ketones in aqueous media are subjected to ultrasonic waves.

Sir: Organometallic compounds, among the most useful reagents in organic chemistry, usually must be prepared in anhydrous solvents due to the rapidity of protonolysis. The presence of water is also known in some cases, e.g., reactions involving magnesium and zinc, to inhibit the formation of the reagent.[1]

We reported some years ago that ultrasonic waves are able to promote the formation of Grignard reagents even in the presence of unusually high concentrations of water.[2] We now report that allylation of aldehydes and ketones can be easily effected in aqueous media in a Barbier-type reaction using zinc as the metal.

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[1] Kharasch, H. S.; Reinmuth, O. "Grignard Reactions of Non-Metallic Substances"; Prentice Hall: New York, 1954; pp 14–15. Nutzel, K. "Methoden der organischer Chemie", Houben Weyl; 4th ed., Muller, E., Ed.; Georg Thieme Verlag: Stuttgart, 1973; Vol 13/2a; pp 553–858.

[2] Luche, J. L.; Damiano, J. C. *J. Am. Chem. Soc.* **1980**, *102*, 7926–7927. See also: Sprich, J. D.; Lewandos, G. S. *Inorg. Chim. Acta* **1983**, *76*, L241–242.

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