sequential treatment of **9a** with $MgBr_2$ at room temperature followed by 1 equiv of CH_3MgI at −70 °C; the isolated yield of **11a** in this case was 80%.

The present method of cyclobutanol formation from epoxides complements and significantly extends that described earlier by Stork and coworkers.[1] An important aspect of the results described herein is that either three- or four-membered rings can be obtained from the same starting materials. Preliminary results in the sulfone series indicate that our conditions, LDA or CH_3MgI, respectively, can be used to synthesize either four- or five-membered rings.[14]

Acknowledgment. Financial assistance from the National Research Council of Canada is gratefully acknowledged.

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(1) (a) G. Stork, L. D. Camma and D. R. Coulson, *J. Am. Chem. Soc.*, **96**, 5268 (1974); (b) G. Stork and J. F. Cohen, *ibid.*, **96**, 5270 (1974).
(2) J. Y. Lallemand and M. Onaga, *Tetrahedron Lett.*, 585 (1975).
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(4) J. H. Babler and A. J. Tortorello, *J. Org. Chem.*, **41**, 885 (1976).
(5) Y. Gaoni, *Tetrahedron Lett.*, 503 (1976).
(6) All new compounds gave NMR and ir spectra consistent with the assigned structures. Exact mass measurements and/or elemental analyses were also obtained.
(7) The concentration of the Grignard reagents was determined by the titration: M. S. Kharasch and O. Reinmuth in "Grignard Reactions of Nonmetallic Substances", Prentice Hall, New York, N.Y., 1954, p 3. When only 1 equiv was used, the reaction produced considerable amounts of iodohydrins in addition to **6**.
(8) Cyclobutanol **6a**, after exchange with D_2O, showed a multiplet from δ 2.3 to 3.0 (4 H) and two quintets showing additional fine structure at 3.39 (1 H) and 4.25 (1 H). In contrast, **5a** showed absorption for its nonaromatic protons at 1.0–1.3 (1 H), 1.4–1.6 (1 H), 1.9–2.7 (1 H), and 3.4–3.8 (3 H).
(9) W. R. Herr and C. R. Johnson, *J. Am. Chem. Soc.*, **92**, 4979 (1970), and references therein.
(10) Reference 7, p 1297.
(11) A competition between the proposed pathways could also account for the deuteration results. However, our results and those of the other workers[1,4,5] suggest that, if an anionic species in formed in the presence of the γ-epoxide, only cyclopropanes are obtained.
(12) NMR data after D_2O exchange for **11a**: δ 2.4–3.5 (5 H), 3.3–3.9 (1 H), and 7.3–7.4 (5 H); ir 3350 and 2230 cm^{-1}. In contrast, **10a** showed NMR peaks at 1.4–2.1 (3 H), 3.4 (2 H), and 6.3 (5 H) after D_2O exchange.
(13) Both diastereomers of the hydroxy NMR ketone **12** were isolated. The less polar isomer (16%) showed NMR peaks at δ 1.96 (3 H), 2.1–2.5 (2 H), 2.8–3.3 (2 H), 4.2 (quintet with fine splitting, 1 H), and 7.1–7.4 (5 H). The more polar isomer (44%) had peaks at 1.92 (3 H), 2.4–3.2 (4 H), 4.18 (quintet, 1 H), and 7.35 (5 H).
(14) J. M. Decesare, B. Corbel, and T. Durst, unpublished observations.
(15) Visitor, France–Canada (N.R.C.) Scientific Exchange Program.

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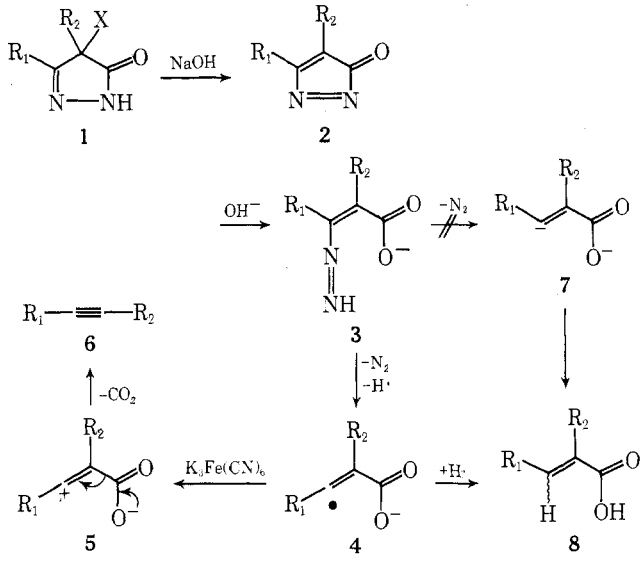
A New Acetylene Synthesis. Junipal

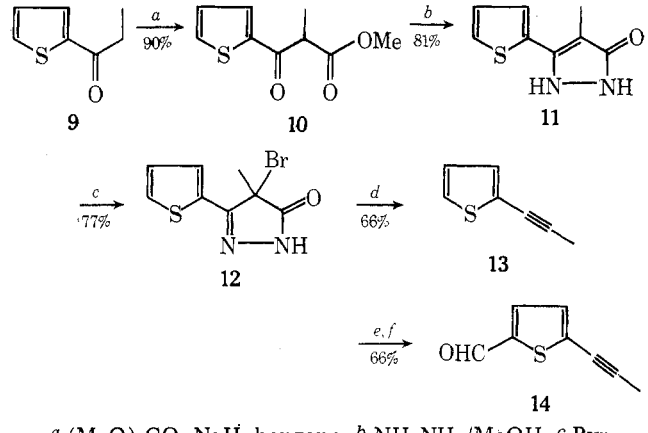
Summary. A new acetylene synthesis involving the reaction of 3,4-disubstituted 4-halo-2-pyrazolin-5-ones with aqueous NaOH in the presence of $K_3Fe(CN)_6$ was applied to the synthesis of junipal [5-(1-propynyl)-thiophene-2-carboxaldehyde].

Sir: The reaction of 3,4-disubstituted 4-halo-2-pyrazolin-5-ones **1** with aqueous NaOH affords a mixture of isomeric α,β-unsaturated carboxylic acids **8** (Scheme I).[1] A previous investigation firmly established the intermediacy of the azacyclopentadienone **2** en route to the acids **8**;[2] however, the fact that an isomeric mixture was obtained in which the *Z* isomer (inversion at C-3) has thus far always predominated is inconsistent with the proposed vinyl carbanion intermediate **7**[2,3] since such an intermediate should protonate in a protic milieu much faster than invert and thereby give the *E* isomer (retention at C-3). We recently suggested the following alternate mechanism[3] to explain the lack of stereoselectivity:

Scheme I



Scheme II



[a] $(MeO)_2CO$, NaH, benzene. [b] NH_2NH_2/MeOH. [c] Pyr·HBr_3/HOAc. [d] NaOH, $K_3Fe(CN)_6/H_2O$. [e] *n*-BuLi, 0 °C. [f] DMF, −78 °C.

extrusion of nitrogen from the vinyl diimide **3** to give a configurationally unstable vinyl radical (e.g., **4**) which can then capture a hydrogen atom to give the isomeric acids **8**. We now report evidence in support of a radical mechanism for the conversion of **1** to **8**, and a modification of the reaction which provides a novel synthesis of disubstituted acetylenes under mild conditions.

If an intermediate vinyl radical **4** were generated with a sufficient lifetime to permit electron abstraction by an appropriate oxidizing agent, then a vinyl carbonium ion **5** might result which could then suffer loss of CO_2 to afford an acetylene **6**. Indeed, the addition of the chloropyrazolinones **1a–e**

Table I. Acetylenes from the Reaction of 4-Chloro-2-pyrazolin-5-ones with Aqueous NaOH–$K_3Fe(CN)_6$

	Chloropyrazolinone 1		
	R_1	R_2	% 6[a,b]
a	Ph	Ph	80
b	Ph	Me	60
c	Me	Ph	12
d	c-C_6H_{11}	Me	25
e	$-(CH_2)_{10}-$		18

[a] Yields represent pure, isolated products. [b] Identified by comparison with authentic samples.

to an aqueous solution containing 5 molar equiv of NaOH and 2 molar equiv of $K_3Fe(CN)_6$ resulted in vigorous gas evolution with concomitant formation of the acetylenes **6a–e**.[4] As can be seen from Table I, this reaction is synthetically useful when the vinyl radical bears an aryl substituent (R_1 = Ph). The diminished yields of acetylenes **6c–e** (R_1 = alkyl) probably reflects a decreased stability (and, hence, lifetime) for the corresponding radicals **4c–e**.

The synthetic potential of this procedure is exemplified by the synthesis of junipal (**14**),[5] an odiferous constituent of the wood-rotting fungus *Daedalea juniperina* (Scheme II) in 24% overall yield from 2-propionylthiophene (**9**).[6] The key step of the synthesis, the oxidative decomposition of the bromopyrazolinone **12**, proceeded in 66% yield to 2-(1-propynyl)thiophene (**13**) which was then converted to junipal[7] by standard procedures[5b] in 66% yield.

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(4) In the absence of the $K_3Fe(CN)_6$, the olefinic acids of **8** are produced in ≥70% yield, whereas the yield of acids is ≤10% when the oxidizing agent is present.
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(7) Mp 81–82 °C (lit.[5b] mp 81–82 °C); ir (CCl_4) 2840, 2810, 2740, 2240, 1670, 1450, 1435, 1215, 1045, and 670 cm^{-1}; NMR (CCl_4) δ 9.7 (s, 1 H), 7.48 (d, 1 H, *J* = 4 Hz), 7.05 (d, 1 H, *J* = 4 Hz), 2.1 (s, 3 H).

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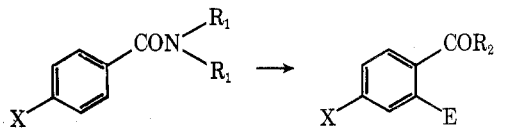
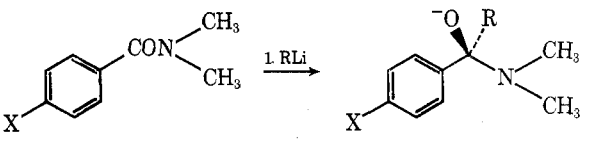
Ortho-Lithiation. A Regiospecific Route to Ortho-Substituted Aryl Ketones

Summary: A method is described to convert *N,N*-dimethylbenzamides directly into ortho-substituted aryl ketones via addition of RLi, followed by ortho-lithiation and reaction with an electrophile.

Sir: To date a direct and general synthesis of ortho-substituted aryl ketones from readily available starting materials has not been reported. The potential route via nucleophilic substitution of the appropriate diazonium salts is limited by the availability of the corresponding anilines. Moreover, such reactions may take a different course, such as the internal cyclization to cinnolines.[1] Alternatively, direct electrophilic substitution of aryl ketones is a formidable problem at best. We here wish to report a practical approach to this problem based on heteroatom directed lithiation. The overall transformation, which is carried out as a one-pot reaction, starts with a tertiary benzamide and leads to the desired ortho-functionalized aryl ketones.

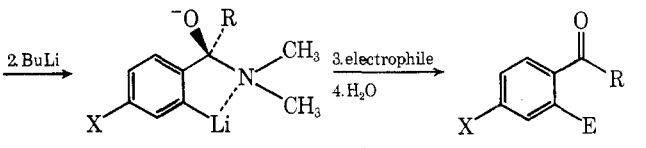


Since dialkylbenzylamines can be lithiated in the ortho position,[2] it was assumed that the tertiary amine in the tetrahedral intermediate **2**, generated by the addition of RLi to a tertiary arylcarboxamide, should also serve as an ortho-directing ligand for a subsequent lithiation. The reaction of



1a, X = Cl
b, X = H

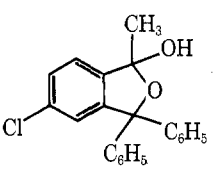
2



3 **4-14**

intermediate **3** with an electrophile followed by aqueous workup then ought to produce the desired ortho-substituted aryl ketone. Tetrahedral intermediates of type **2** have provided regiospecificity in the α-metalation of thiophenes[3-5] and furans,[6] as reported by two separate groups. This superficially can serve as precedent for our postulate. However, since it has been well established that the α positions of five-membered heterocycles are generally deprotonated much more readily than benzenoid systems,[7] it was by no means certain that the desired metalation could be realized. It was, therefore, not only of theoretical, but, as indicated at the outset, of considerable practical interest to test the feasibility of this concept.

The reaction works remarkably well, and, although the isolated yields are not spectacular,[8] they are quite respectable considering the number of operations actually carried out. As indicated in Table I, the method is quite general in terms of the nature of both RLi (step 1) and the electrophile (step 3). It should be pointed out that, in cases where the newly introduced ortho substituent E can serve as an internal nucleophile, cyclic products are isolated exclusively as documented by entries **9**, **12**,[9] and **13**. Another item deserving special attention is the high degree of regioselectivity attained in the preparation of **7**. Whereas in principle deprotonation could occur in either of the two phenyl rings (R = C_6H_5) during the metalation step (2), the rate-enhancing effect of



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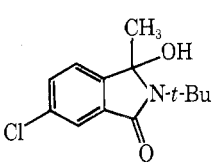

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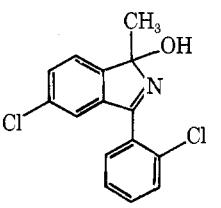

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