Carbonium Ions. XXIII. Chain Elongation in the Rearrangement of 2,3-Dimethyl-4-penten-2-ol to 2-Methyl-3-hexen-2-yl Cation

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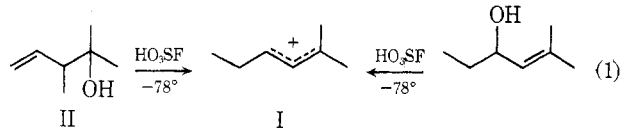
Received September 25, 1974

The 2-methyl-3-hexen-2-yl cation (I) is formed on addition of 2,3-dimethyl-4-penten-2-ol (II) to HO_3SF at −78°, eq 1. Ion I is the dominant product as evidenced by 90% of



II I (1)

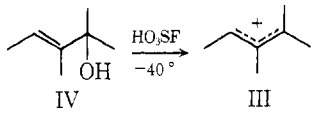
the nmr band areas being attributable to I. A novel feature of eq 1 is the elongation of the five-carbon chain of II to the six-carbon chain of I. This type of elongation does not seem to have been observed heretofore in allyl cation rearrangements[1] and will probably be uncommon because it would involve going from more branched to less branched carbonium ions.

The rearrangement cannot have taken place by H migration alone and paths involving H migration and 1,2-alkyl shifts are unlikely. The only attractive paths are those involving cyclopropylcarbonium ions and rearrangements of these ions of the type exemplified by the scrambling of methylene groups in the cyclopropylmethyl cation.[2] At least two paths involving this type of rearrangement can be constructed.

Structure I was assigned on the basis of its nmr spectrum: triplet at 1.29 (J = 6.5 Hz, ~3 H on C-6), unresolved quartet at 2.96 (2.0 H on C-5), singlet at 3.06 (6.0 H on *gem*-dimethyl), doublet at 7.74 (J = 14.5 Hz, 1.0 H on C-2), doublet at 9.60 (J = 14.5 Hz, 1.0 H on C-3). The band at 9.60 was broadened by coupling with the H on C-4. The band positions are in accord with precedent.[1]

The identification of I was confirmed by its independent synthesis by addition of 5-methyl-4-hexen-3-ol to HO_3SF at −78°, eq 1. This formation was quantitative.

It had been anticipated that II would form the 2,3-dimethyl-3-penten-2-yl cation, III, as the first stable observable cation. The question thus arose as to whether III was an intermediate in the formation of I. This was not the case. Addition of 2,3-dimethyl-3-penten-2-ol (IV) to HO_3SF at −40° produced III, eq 2. Ion III was stable at



IV III (2)

−40°. On warming to 25° it formed a mixture of cyclopentenyl cations (as did I) without the nmr bands of I ever appearing. This formation of cyclopentenyl cation mixtures is a common fate of carbonium ions.[3]

The identification of III rested on its mode of formation and nmr spectrum: singlet at 2.23 (3.0 H on C-3), a broad unresolved pair of bands at 2.75 (6.0 H of the *gem*-dimethyl), doublet at 3.11 (J = 6 Hz, 3.1 H on C-5), quartet at 9.55 (J = 6 Hz, 1.0 H on C-4). These are typical for allyl cations[1] and are in agreement with structure III.

It is remarkable that the two alcohols II and IV, which differ only in the position of the double bond, produce entirely different stable allyl cations, I AND III, on addition to HO_3SF at −78°.

Experimental Section

Nmr Spectra. Spectra were recorded on a Varian A-60 instrument. Spectra of ions I and III were recorded at −40°. Tetramethylammonium chloride (δ 3.10) was used as the internal standard in HO_3SF. Band positions are expressed in δ.

Carbonium Ion Precursors. 2,3-Dimethyl-4-penten-2-ol (II) was commercially available from Aldrich Chemical Co., Milwaukee, Wis. 2,3-Dimethyl-3-penten-2-ol[4] (IV) was prepared from CH_3Li and 3-methyl-3-penten-2-one. The nmr spectrum in CCl_4 consisted of a singlet (6 H, *gem*-dimethyl) at 1.22, an overlapping singlet and doublet (6 H, remaining two methyl groups) at 1.45–1.77, a singlet (H on OH) at 2.47, and a multiplet (H on C-4) from 5.20 to 5.77. The J coupling constants between hydrogens on C-4 and C-5 could not be accurately determined but both were in the same 6–7-Hz range. The boiling point (82–83° at 72 Torr) was in agreement with that reported (84–86° at 85 Torr[4]).

5-Methyl-4-hexen-3-ol[5] was prepared by $LiAlH_4$ reduction of 5-methyl-4-hexen-3-one. The nmr spectrum in CCl_4 consisted of a triplet (J = 6.5 Hz, 3 H on C-6) at 0.83, a multiplet (2 H on C-5) from 1.06 to 1.62, a pair of doublets (J = 1.5 Hz, 6 H on *gem*-dimethyl) at 1.65 and 1.70, a singlet (H on OH) at 3.07, a multiplet (H on C-4) from 3.93 to 4.35, and a multiplet (H on C-3) from 4.95 to 5.27. The boiling point (58° at 13 Torr) was in agreement with that reported (63–65° at 22 Torr[5]).

Acknowledgments. Support of this work by the donors of the Petroleum Research Fund, administered by the American Chemical Society, and by the National Science Foundation is gratefully acknowledged.

Registry No.—I, 53567-43-4; II, 19781-52-3; IV, 53555-58-1; 3-methyl-3-penten-2-one, 565-62-8; 5-methyl-4-hexen-3-ol, 53555-59-2; 5-methyl-4-hexen-3-one, 13905-10-7.

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A New Method for the Preparation of 4-Acylpyrazoles. The Reaction of C(α),N Dianions of Phenylhydrazones with Acid Chlorides

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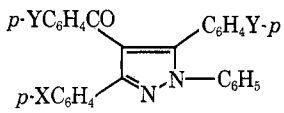
Received September 6, 1974

The 1,4 dianions of phenylhydrazones having an α-hydrogen atom, such as dilithioacetophenone phenylhydrazone, have been condensed with esters[1] and nitriles[2] to give, after acid cyclization, numerous pyrazoles, especially 3,5-disubstituted pyrazoles.

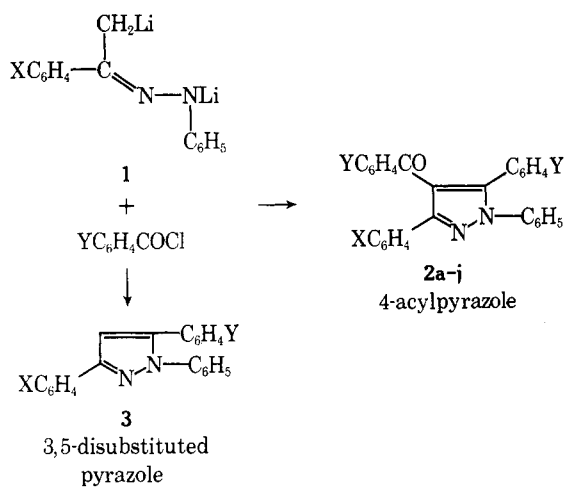
It was of interest to treat these dianions with aroyl chlorides in order to determine the effect of these more reactive electrophilic reagents and to compare the results with those already obtained for esters and nitriles. When the dilithiophenylhydrazones 1 were treated with benzoyl, *p*-chlorobenzoyl, and *p*-toluoyl chlorides, followed by acid cyclization, 4-acylpyrazoles **2a–j** were obtained instead of 3,5-disubstituted pyrazoles **3**.

Table I
4-Acylpyrazoles

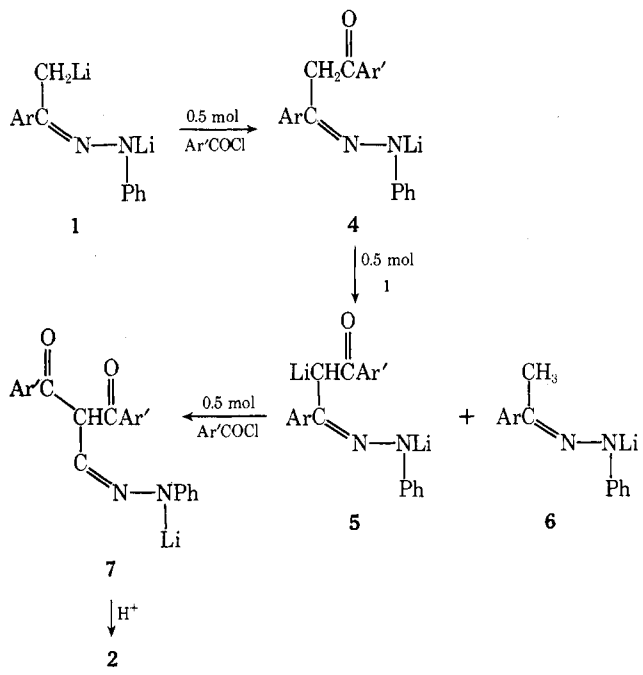


Compd no.[a]	X	Y	Name (-pyrazole)	Yield, %	Mp, °C	Ir (C=O),[b] cm^{-1}
2a	H	H	4-Benzoyl-1,3,5-triphenyl-	100	174–176[c]	1650–1655
2b	H	Cl	4-(*p*-Chlorobenzoyl)-5-(*p*-chlorophenyl)-1,3-diphenyl-	38	169–170	1640–1650
2c	H	CH_3	1,3-Diphenyl-4-(*p*-toluoyl)-5-(*p*-tolyl)-	62	166–167	1640–1650
2d	F	Cl	4-(*p*-Chlorobenzoyl)-5-(*p*-chlorophenyl)-3-(*p*-fluorophenyl)-1-phenyl-	32	177–179	1640–1650
2e	F	H	4-(Benzoyl)-1,5-diphenyl-3-(*p*-fluorophenyl)-	68	143–144	1640–1650
2f	CH_3	H	4-(Benzoyl)-1,5-diphenyl-3-(*p*-tolyl)-	72	170–172	1640–1650
2g	Cl	H	4-Benzoyl-1,5-diphenyl-3-(*p*-chlorophenyl)-	43	153–156	1645–1655
2h	Cl	CH_3	3-(*p*-Chlorophenyl)-1-phenyl-4-(*p*-toluoyl)-5-(*p*-tolyl)-	30	184–186	1640
2i	CH_3	CH_3	1-Phenyl-4-(*p*-toluoyl)-3,5-di(*p*-tolyl)-	61	158–160	1640
2j	CH_3O	Cl	3-(*p*-Anisyl)-4-(*p*-chlorobenzoyl)-5-(*p*-chlorophenyl)-1-phenyl-	47	162–164	1650

[a] C, H, N analysis for **2b–j** ± 0.30%. [b] The C=O absorption for 4-acylisoxazoles was reported at 1653 cm^{-1} (KBr pellets); see ref 5. [c] Lit. mp 174°; N analysis, ±0.30%; see ref 4.



Scheme I



In a typical reaction, a freshly prepared phenylhydrazone was dissolved in tetrahydrofuran and treated with 2 molar equiv of *n*-butyllithium in hexane, and this was followed by condensation with 1 molar equiv of aroyl chloride, acid cyclization with 3 *N* hydrochloric acid, and recrystallization of the product. Optimum yields of products were obtained when the ratio of phenylhydrazone:base:acid chloride was 1:2:1; this is consistent with the proposed mechanism. The yield is based on one-half of the amount of acid chloride used, since two molecules of this reactant are needed for each molecule of 4-acylpyrazole prepared.

The sequence in Scheme I would account for the results obtained. Reaction of the phenylhydrazone with 2 equiv of *n*-butyllithium gives $C(\alpha)$,*N*-dilithiophenylhydrazone **1**. Prior to the addition of the full amount of the base, the reaction mixture was red in color, and it turned dark red to red-black in color after addition was complete, indicating complete conversion to dianion **1**. Treatment of **1** with 0.5 equiv of acid chloride leads to intermediate **4**, which with 0.5 molar equiv of dianion **1** gives **5** and **6**. Reaction of **5** with another 0.5 equiv of acid chloride, which was slowly being added to the reaction mixture, would lead to intermediate **7** and thence to **2**.

It was of interest to treat a phenylhydrazone with 1 molar equiv of base followed by 1 molar equiv of acid chloride. When acetophenone phenylhydrazone monoanion was treated with benzoyl chloride, and was followed by acid cyclization, **2a** was isolated in 16% yield. This suggests formation of some $C(\alpha)$ ion in addition to the resonance stabilized N anion;[3] however, other monolithiophenylhydrazones treated with acid chlorides gave side products (unidentified, but definitely not pyrazoles), which supports the importance of the $C(\alpha)$,*N*-dilithiophenylhydrazone intermediate.

Only 5-(*p*-anisyl)-3-(*p*-tolyl)pyrazole resulted from the treatment of the dianion with *p*-anisoyl chloride followed by cyclization. The failure to form the 4-acylpyrazole evidently reflects the diminished reactivity of the acid chloride, which does not react further with intermediate **5** to give **7**.

Of the 4-acylpyrazoles, only **2a** has been reported, and it was prepared by the reaction of benzoyl chloride with 1,3,5-triphenylpyrazole.[4] The melting point of **2a** prepared in this work agreed with that reported (see Table I). The

carbonyl absorption for all of the 4-acylpyrazoles prepared was in the range of 1640–1655 cm^{-1}, comparing well with the values reported for 4-acylisoxazoles.[5]

This new route to 4-acylpyrazoles requires readily available starting materials, is easily and readily carried out, and products are easily purified.

Experimental Section

All combustion analyses were performed by Robertson Laboratory, Florham Park, N.J., and by M-H-W Laboratories, Garden City, Mich. Infrared spectra were obtained from a Perkin-Elmer 700 infrared spectrometer (0.1 mm, chloroform solvent). Melting points were taken in a Thomas-Hoover melting point apparatus in open tubes and are uncorrected. The *n*-butyllithium was obtained from the Lithium Corporation of America, Bessemer City, N.C. The tetrahydrofuran was obtained from Matheson Coleman and Bell and was used as supplied. The phenylhydrazones were prepared by a standard method,[6] recrystallized from ethanol, and used immediately.

General Procedure for the Preparation of 4-Acylpyrazoles. To a stirred solution of 0.02 mol of phenylhydrazone dissolved in 100 ml of dry THF, which was blanketed by nitrogen and cooled to 0°, was added 0.042 mol of *n*-butyllithium during 5 min. After stirring the resulting mixture for 30 min, 0.022 mol of acid chloride dissolved in 100 ml of THF was added during 5–10 min. The resulting mixture was stirred for 30 min and neutralized with 100 ml of 3 *N* HCl. The entire mixture was stirred and heated under reflux for 1 hr and cooled. The mixture was placed in a large flask and approximately 100 ml of ether was added, and this was followed by careful neutralization with sodium bicarbonate. The layers were separated, and the aqueous layer was extracted with two 50-ml portions of ether. The organic layers were combined, dried (Na_2SO_4), filtered, and concentrated, and the resulting oil or residue was immediately crystallized and/or recrystallized from hot 95% ethanol.

Preparation of 3-(*p*-Methoxyphenyl)-5-(*p*-tolyl)pyrazole. Dianion (0.025 mol) was prepared by the treatment of 0.025 mol of 4-methylacetophenone phenylhydrazone with 0.055 mol of *n*-butyllithium (see above). This dianion was condensed with 0.05 mol (twofold excess) of *p*-anisoyl chloride dissolved in 100 ml of THF. After acid cyclization and isolation of product, 5.00 g (59%) of 3-(*p*-methoxyphenyl)-5-(*p*-tolyl)pyrazole was obtained: nmr ($CDCl_3$) δ 2.38 (s, 3 H, CH_3), 3.78 (s, 3 H, CH_3O), 6.72 (s, 1 H, C_4H), and 6.88–7.88 (m, 13 H, ArH). *Anal.* Calcd for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.23. Found: C, 80.98; H, 5.92; N, 8.09.

Acknowledgment. This work was supported at Newberry College by grants from the Petroleum Research Fund, which is administered by the American Chemical Society, and the South Carolina Heart Association, Inc. The Public Health Service, Research Grant CA-04455, supported the work at Duke University. The use of the A-60 nmr spectrometer and the cooperation of Dr. R. Cargill, at the University of South Carolina, are gratefully acknowledged.

Registry No.—**1a** dianion, 13636-57-2; **1d** dianion, 53608-33-6; **1f** dianion, 53608-34-7; **1g** dianion, 53608-35-8; **1j** dianion, 53608-36-9; **2a**, 53608-37-0; **2b**, 53608-38-1; **2c**, 53608-39-2; **2d**, 53608-40-5; **2e**, 53608-41-6; **2f**, 53608-42-7; **2g**, 53608-43-8; **2h**, 53608-44-9; **2i**, 53608-45-0; **2j**, 53608-46-1; benzoyl chloride, 98-88-4; *p*-chlorobenzoyl chloride, 122-01-0; *p*-toluoyl chloride, 874-60-2; *p*-anisoyl chloride, 100-07-2; 5-(*p*-anisyl)-3-(*p*-tolyl)pyrazole, 53608-47-2.

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Acid-Catalyzed Rearrangement of 20-Vinylpregn-5-ene-3β,20-diol 3-Acetate[1]

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Received September 6, 1974

There are many reports that C-20 tertiary carbinol steroids may undergo dehydration,[2] rearrangement,[3] or both[4] under certain conditions.

A recent report by Narwid, Cooney, and Uskoković[5] on the Carroll rearrangement of (20*S*)-20-vinylpregn-5-ene-3β,20-diol 3-acetate (**2a**) prompts us to publish our results on the acid-catalyzed rearrangement of that compound. This work was undertaken in order to compare the behavior of the 20-vinyl- with the behavior of the 2-methyl-[3] and 20-ethynylcarbinols[4] under similar conditions.

The synthesis of 20-vinylpregn-5-ene-3β,20-diol 3-acetate (20-isomeric mixture) (**2a,b**) was achieved by treating 3β-hydroxypregn-5-en-20-one acetate (**1**) with vinylmagnesium bromide, followed by reacetylation[6] of the 3β-hydroxyl. The epimers **2a** and **2b** were isolated in an 11:1 ratio. The 20*S* configuration was assigned to the major product **2a** (77%) for the following reasons. (1) In a recent publication,[7] we have shown that the stereochemistries of nucleophilic additions of 20-keto steroids are in agreement with Cram's rule. (2) The (20*S*)-20-ethynylpregn-5-ene-3β,20-diol 3-acetate (**5**),[4,8] when selectively reduced with Lindlar catalyst,[9] gave a product identical in all respects with the vinylcarbinol **2a**.

The present study is concerned solely with acid-catalyzed reactions of the vinylcarbinol **2a**. The compounds isolated were those arising from dehydration and allylic rearrangement; no D-homoannulation was observed (Scheme I). Table I summarizes the results of this investigation.

Table I
Reaction of Carbinol 2a

Reagents, conditions	Products in % yield		
	3	4b	7
AcOH–*p*-TsOH, 25°, 72 hr	20	50	
AcOH–I_2, 100°, 0.5 hr	10	50	
$POCl_3$–Py, 100°, 3 hr	30		
H_2SO_4–dioxane, 100°, 1 hr	80		
AcOH–*p*-TsOH, 100°, 0.25 hr		30	60
Benzene–PBr_3, 25°, 20 hr		70	

Structure of Triene 3. The elemental analysis of **3** showed that the compound was derived by loss of one molecule of water from the vinylcarbinol **2a** and the infrared spectrum showed the absence of any hydroxyl group. The ultraviolet absorption maximum was at 228 nm (ε 11,500), characteristic of a monosubstituted conjugated diene,[10,11] although higher than predicted according to Woodward's[12] rules. The proton magnetic resonance spectrum showed the presence of six vinylic protons and the absence of a methyl group on an unsaturated carbon, consistent with the structure **3**.

Structure of Diacetate 4b. The elemental analysis of **4b** indicated a formula derived from the starting material **2a** by acetylation of the alcoholic function. This was confirmed by the absence of any hydroxyl band in its infrared