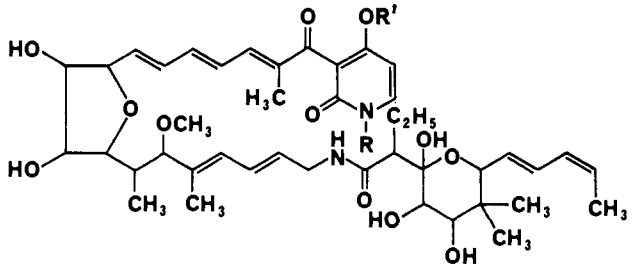


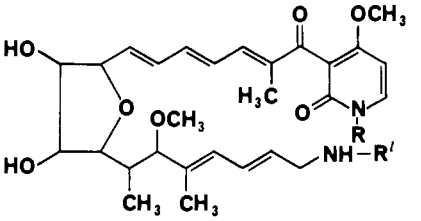
1, R = R′ = H (mocimycin)
1a, R = H; R′ = CH_3 (mocimycin methyl ether)
2, R = CH_3; R′ = H (antibiotic X-5108)
2a, R = R′ = CH_3 (antibiotic X-5108 methyl ether)
2b, R = CH_3; R′ = 4-BrBzl (antibiotic X-5108 4-bromobenzyl ether)

Recently, two new antibiotics, mocimycin (Delvomycin)[4-6] and kirromycin,[7,8] were described whose biological and physicochemical properties suggested similarity to antibiotic X-5108. Mocimycin and kirromycin could be clearly differentiated from antibiotic X-5108 by various tlc systems but not from each other. The nmr spectra of the three antibiotics were similar, but the spectrum of antibiotic X-5108 was distinguished by the presence of a signal for an *N*-methyl group which was absent in the spectra of both mocimycin[6] and kirromycin, suggesting close structural similarity or identity of mocimycin and kirromycin. Mocimycin was identified as des-*N*-methyl antibiotic X-5108 on the basis of the following observations.

Mocimycin sodium salt, $\delta_{TMS}^{CD_3OH}$ 3.17 (s, CH_3OCH), treated with methyl iodide, afforded a mixture of amorphous mono- and dimethylated products **1a** ([α]D −94° (*c* 0.9, ethanol), λ_{max} (ϵ) 207 (51,000), 231 (58,850), ~290 infl (16,050), and 334 nm (38,750) in 0.1 *N* HCl; 207 (51,200), 232 (60,100), ~290 infl (16,050) and 334–335 nm (39,200) at pH 7; 232 (62,900), ~290 infl (16,500), and 329 nm (40,500) in 0.1 *N* KOH; $\delta_{TMS}^{CD_3OD}$ 3.13 (s, CH_3OCH) and 3.83 (s, CH_3OC$\lessgtr$)) and **2a**, respectively ([α]D −93° (*c* 0.9, ethanol), λ_{max} (ϵ) 210–211 (53,200), 232–233 (58,500), ~297–298 infl (18,600), and 336 nm (40,000) in 0.1 *N* HCl; 210–211 (54,500), 232–233 (59,300), ~298–299 infl (18,600), and 336 nm (39,900) at pH 7; 232–233 (58,850), ~297–298 infl (18,600), and 336 nm (40,000) in 0.1 *N* KOH; $\delta_{TMS}^{CD_3OD}$ 3.13 (s, CH_3OCH), 3.49 (s, CH_3N), and 3.79 (s, CH_3OC$\lessgtr$)).

Continued methylation of **1a** with methyl iodide or dimethyl sulfate yielded **2a**, also obtained directly as a major product by reaction of mocimycin sodium salt with dimethyl sulfate, identical in all respects with **2a** derived from antibiotic X-5108. Further, mocimycin derivatives **1a** and **2a** were treated with acetic acid, each yielding goldinono-1,4-lactone-3,7-hemiketal,[3] as well as amorphous **3** acetate ([α]D −53.5° (*c* 0.6, 90% ethanol); λ_{max} (ϵ) 236–237 (35,300), ~290 infl (14,700) and 330–331 nm (40,000) in 0.1 *N* HCl and 237 (33,200), ~290 infl (15,200), and 334–336 nm (39,650) in 0.1 *N* KOH and at pH 7; $\delta_{TMS}^{CD_3OD}$ 3.17 (s, CH_3OCH) and 3.84 (s, CH_3OC$\lessgtr$)) and amorphous **4** acetate, respectively ([α]D −49° (*c* 1.0, ethanol), λ_{max} (ϵ) 210 (43,200), 237–238 (33,750), ~298 infl (19,200), and 335–336 nm (39,400) in 0.1 *N* HCl and 210 (43,200), 237–238 (33,000), ~298 infl (18,600), and 335–336 nm (38,660) at pH 7; 237–238 (34,000), ~298 infl (18,600), and 335–336 nm (38,900) in 0.1 *N* KOH; $\delta_{TMS}^{CDCl_3}$ 3.17 (s, CH_3OCH), 3.50 (s, CH_3N), and 3.77 (s, CH_3OC$\lessgtr$)).

Goldinamine methyl ether (**4**) was converted to **4a**, whose composition of $C_{31}H_{39}F_3N_2O_8$ was confirmed by mass spectrometry. Similarly, acylation of **3** gave **3a**, $C_{30}H_{37}F_3N_2O_8$, with nmr and mass spectra consistent with the proposed structure.



3, R = R′ = H (des-*N*-methyl goldinamine methyl ether)
4, R = CH_3; R′ = H (goldinamine methyl ether)
3a, R = H; R′ = $COCF_3$
4a, R = CH_3; R′ = $COCF_3$

Compounds **4** and **4a**, derived from mocimycin, proved to be identical in all respects, including a comparison of CD spectra, with goldinamine methyl ether (**4**) and its *N*-trifluoroacetyl derivative **4a** prepared from antibiotic X-5108. In addition, periodate oxidations of **4**, derived from both mocimycin and antibiotic X-5108, afforded two products each, *threo*-8-amino-3-methoxy-2,4-dimethyl-4(*trans*),6(*trans*)-octadienal[1] with undetermined but identical absolute stereochemistry in both preparations as suggested by identical CD spectra of the *N*-acetyl derivatives, and 8-[4-methoxy-1,-2-dihydro-1-methyl-2-oxo-3-pyridyl]-7-methyl-8-oxo-2(*trans*),4(*trans*),6(*trans*)-octatrienoic acid, mp 220–223° dec, exhibiting uv and nmr spectra similar to its 4-bromobenzyloxy analog.[9,10]

(4) R. Beukers, J. G. Oostendorp, and C. J. van Eeken, Abstracts, Second World Congress on Animal Feeding, Madrid, Oct 23–28, 1972, p 127.
(5) E. J. van Weerden, P. van der Wal, and J. B. Schutte, ref 4, p 133.
(6) C. Vos and P. E. J. Verwiel, *Tetrahedron Lett.*, 2823 (1973).
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(8) We are indebted to Professor Zähner for a 50-mg sample of crude kirromycin. This sample was purified prior to analysis.
(9) H. Maehr, J. F. Blount, M. Leach, and A. Stempel, *Helv. Chim. Acta*, 55, 3054 (1972).
(10) Note Added in Proof. The designation "goldinodox" is being proposed as a nonproprietary name for antibiotic X-5108.

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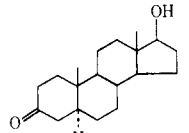
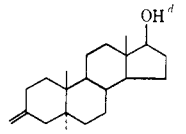
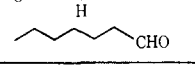
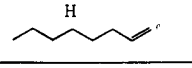
Fragmentation Reaction of Ylides. III. A New Synthetic Route for Exo Methylenes

Sir:

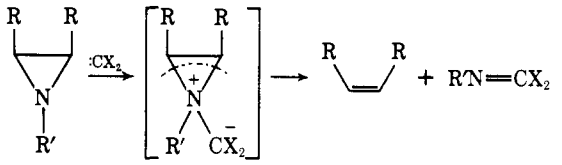
N-Alkylaziridines react with dihalocarbenes to give the corresponding olefins by breaking the two C–N bonds in the aziridine ring. The reaction is highly stereospecific and the relative configuration of substituent groups is retained completely in the olefins.[1] We have previously suggested[1a] that the reaction gives aziridinium ylide as the initial intermediate, which then decomposes to the olefin by a cheletropic reaction.[2]

(1) (a) Y. Hata and M. Watanabe, *Tetrahedron Lett.*, 3827 (1972); (b) Y. Hata and M. Watanabe, *ibid.*, 4659 (1972).
(2) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, New York, N. Y., and London, 1970, p 152.

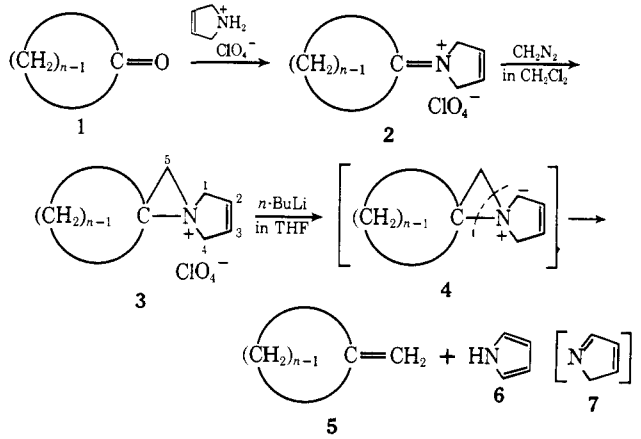
Table I. Products and Their Yields from the Decomposition of Aziridinium Ylides

Ketones **1**	Products **5**	% yield of last step **3** → **5**	% total yield[f] of **5**	% yield of **5** by $Ph_3P{=}CH_2$
	 [a]	Quantitative	71	52[a]
	 [b]	40	38	5–10[h]
	 [c]	80	64	
	 [d]	*g*	82	38[d,i]
	 [e]	81	68	

[a] G. Wittig and V. Schöllkopf, *Ber.*, **87**, 1318 (1954). [b] R. B. Turner and R. H. Garner, *J. Amer. Chem. Soc.*, **80**, 1424 (1958). [c] T. D. Nevitt and G. S. Hammond, *ibid.*, **76**, 4124 (1954). [d] F. Sondheimer and R. Mechoulam, *ibid.*, **79**, 5029 (1957). [e] Commercially available. [f] Based on the initial amount of corresponding 3-pyrroline perchlorate used. [g] No isolation of spiroaziridinium salt **3**. [h] A. Schriesheim, R. J. Muller, and C. A. Rowe, Jr., *J. Amer. Chem. Soc.*, **84**, 3164 (1962). [i] When the reaction product had a high melting point, *e.g.*, a steroid, isolation of the product was simpler than in the Wittig-type reaction. After treatment of the reaction mixture with water and extracting with ether, stripping off the solvent immediately gave crude crystals of 3-methylene-5α-androstan-17β-ol. This was recrystallized from methanol to pure **5**, mp 145°.



Another method of preparing an ylide is the abstraction of a hydrogen atom from the position adjacent to a quaternary nitrogen atom. We therefore considered that if it were possible to abstract the hydrogen atom from C_1 of aziridinium salt **3**, we should obtain the exo-



methylene **5** through decomposition of spiro ylide **4**. We have examined this assumption and report here a new synthetic route for exo methylenes from carbonyl compounds.

Immonium salt **2** and spiro salt **3** were readily prepared by reported procedures.[3] Since hydrogen atoms on small ring carbon compounds usually have increased acidity due to the strain-induced increase in electronegativity of the carbon atom,[4] the secondary amine used to prepare the immonium salt **2** should have more active hydrogens on the carbons adjacent to the nitrogen atom. Among the many compounds studied, 3-pyrroline was the most suitable amine. *n*-BuLi gave the best results as the strong base used to remove a hydrogen from **3** to form ylide **4**. By this procedure we obtained a good yield of exo-methylenes **5** and pyrrole, **6**, as reaction products from the ketones described in Table I. The structure of exo-methylenes **5** was determined by comparison with an authentic sample prepared according to the references cited under Table I. From consideration of the reaction sequence, pyrrolein, **7**, should be the primary product. However, we detected only pyrrole, **6**, as the basic component. Pyrrolein should be converted into pyrrole immediately after production in the reaction solution. The procedure used with cyclohexanone is described as a typical example of the reaction.

On mixing 3-pyrroline perchlorate[5] and cyclohexanone, immonium salt **2** (n = 6) was immediately formed as white crystals (89%).[6] The product was washed with ether to remove excess ketone and used as such for the next step. Recrystallization of a sample of crude **2** from EtOAc–CH_3CN gave fine crystals of mp 220–223°: nmr (DMSO) δ 6.1 (2 H, s, –CH=), 4.75 (4 H, s, $-CH_2N^+$), 2.76 (4 H, m, $-CH_2C{=}$), 1.7 (6 H, m, CH_2); ir 1665 cm^{-1} ($C{=}N^+$).

Crude immonium salt **2** dissolved in CH_2Cl_2 was converted to the spiro salt **3** (n = 6) using diazomethane at −10°.[7] A crystallized sample of the product showed mp 123–124°: nmr (DMSO) δ 5.85 (2 H, 2, –CHC=), 4.2 (4 H, s, $-CH_2N^+$), 3.3 (2 H, s, CH_2), 1.5 (10 H, m, CH_2). A solution of crude spiro salt **3** in a few milliliters of THF was treated with an excess of *n*-BuLi–

(3) (a) N. J. Leonard, K. Jann, J. V. Paukstelis, and C. K. Steinhardt, *J. Org. Chem.*, **28**, 1499 (1963); (b) N. J. Leonard and J. V. Paukstelis, *ibid.*, **28**, 3021 (1963).

(4) Y. Hata, "The Chemistry of Highly Strained Compounds," Kagakudozin, Osaka, 1970, p 82.

(5) Commercially available 3-pyrroline was used. The perchlorate salt was prepared according to ref 3b.

(6) If a large amount of liquid ketone was used, no other solvent was necessary. If the stoichiometric amount of liquid or solid ketone was used, a solvent was required. In such case acetonitrile was best. The yield of **2** was nearly independent of the amount of solvent.

(7) The amount of diazomethane and the reaction time were the same as described in ref 3b.

hexane under ice cooling.[8] When the reaction was complete water was added and the methylenecyclohexane formed was analyzed by vpc using ethylbenzene as internal reference. The yield was 71% (based on 3-pyrroline perchlorate). In another experiment, decomposition of pure spiro salt **3** with *n*-BuLi gave a quantitative yield of methylenecyclohexane. Other examples tried are summarized in the Table I.

(8) *Ca.* 1.5 or 2.0 mol of *n*-BuLi–hexane was used. A few minutes after the crystals of **3** had disappeared and the reaction finished, the reaction mixture became thick by the deposition of $LiClO_4$.

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1,3-Dipolar and Diels–Alder Reactions of Reissert Salts with Stilbenes and Tolans

Sir:

Although freshly prepared hydrofluoroborate salts of 2-acyl-1,2-dihydroisoquinaldonitriles (Reissert compounds[1]) usually have the structure **1**, they readily isomerize to **3** and **4** in solution by way of the mesoionic intermediate **2**.[2] 1,3-Dipolar addition reactions of these salts with reactive acetylenic 1,3-dipolarophiles, such as dimethyl acetylenedicarboxylate, ethyl phenylpropiolate, and ethyl tetrolate, have been shown to take place in high yields.[3-5] Also, complex condensation–rearrangement reactions of these salts, the initial step of which is thought to be a Diels–Alder reaction involving **4**,[6] have been shown to occur with reactive olefinic dienophiles, such as ethyl cinnamate, dimethyl maleate, and ethyl acrylate.[7,8]

In all of the reactions studied up to the present time, the Reissert salts have given only 1,3-dipolar addition products with alkynes and only the complex condensation–rearrangement products with alkenes. We considered this to be somewhat unusual, inasmuch as both 1,3-dipolar addition reactions and Diels–Alder reactions are known to occur with either alkenes or alkynes. Furthermore, the rates of 1,3-dipolar addition reactions of sydnones and munchnones with structurally similar alkenes and alkynes are not greatly different.[9]

We have now carried out reactions of 2-benzoyl-1,2-dihydroisoquinaldonitrile hydrofluoroborate (**1**, R = C_6H_5) with stilbene and tolan. The reaction of **1** (R = C_6H_5) with stilbene was carried out in DMF solution at 100° for 18 hr, and there was obtained the known[10,11] 2-(1-isoquinolyl)-3,4,5-triphenylpyrrole (**10**, R = C_6H_5) in 34% yield, but no trace of a product of a 1,3-dipolar addition reaction could be found. The reaction of **1** (R = C_6H_5) with tolan was carried out in refluxing DMF solution (*ca.* 153°) for 24 hr, and there was obtained a mixture of products, which included 1,2,3-triphenylpyrrolo[2,1-*a*]isoquinoline (**12**, R = C_6H_5), mp 178–179°, 2-(1-isoquinolyl)-3,4,5-triphenylpyrrole (**10**, R = C_6H_5), and isoquinaldonitrile (**11**). Unreacted tolan, which had been used in threefold excess, was recovered in 82% yield, and the yields of **12**, **10**, and **11**, based on the amount of **1** (R = C_6H_5) used, were 28, 6.4, and *ca.* 1%, respectively. We were able to show conclusively, by means of control experiments, that **10** (R = C_6H_5) arose from the reaction of **1** (R = C_6H_5) with tolan, and that its formation was not attributable to the presence of a small amount of stilbene, as an impurity, in the tolan. Thus, for the first time, we have found evidence for competing 1,3-dipolar addition and Diels–Alder condensation reactions of a Reissert salt.

In order to obtain an estimate of the relative rates of the competing 1,3-dipolar and condensation–rearrangement sequences, a mixture of 8.64×10^{-2} mol of *trans*-stilbene, 8.64×10^{-2} mol of tolan, and 2.88×10^{-3} mol of **1** (R = C_6H_5) was heated in DMF solution at 100° for 24 hr. There was obtained 0.73 g (60%) of **10** (R = C_6H_5) and 0.16 g (14%) of **12** (R = C_6H_5). Thus, the approximate rate ratio of the Diels–Alder condensation–rearrangement sequence to the 1,3-dipolar addition sequence was about 4, this value being corrected for the relatively small amount of **10** (R = C_6H_5) formed in the reaction of **1** (R = C_6H_5) with tolan.

The mechanisms of the 1,3-dipolar addition reactions[3-5] and of the complex condensation–rearrangement reactions[6,10] have been depicted elsewhere. We tentatively suggest that the mechanism of the reaction by which **10** (R = C_6H_5) and **11** are obtained from **1** (R = C_6H_5) and tolan is that shown in Scheme I. A key step in this overall transformation is the transfer of a hydride ion from 2-benzoyl-1,2-dihydroisoquinaldonitrile, which is present in equilibrium with **1** (R = C_6H_5), to the intermediate carbonium ion **8**, a precursor of **10**.

In the light of these results, we are now able to provide an explanation for the fact that alkenes ordinarily give complex condensation–rearrangement products which arise from Diels–Alder adducts in reactions with **1**, while alkynes ordinarily give 1,3-dipolar addition products, or compounds derived from them. We have already demonstrated[5] that the reaction between **1** (R = C_6H_5) and ethyl phenylpropiolate in DMF–ethanol solution at 41° is a second- and first-order reversible one, and it is well known that Diels–Alder reactions are reversible. Thus, it is reasonable to assume that the equilibrium mixture of **1**, **2**, **3**, and **4** undergoes the initial steps of both types of reaction with both alkenes and alkynes. With alkynes, however, the subsequent pathway to form a fully aromatic heterocyclic product *via* the 1,3-dipolar addition intermediate (which involves merely loss of isocyanic acid from a bridged adduct[3,4]) has a smaller overall free energy of activation than the conversion of the Diels–Alder adduct of type **5** to the final, fully aromatic product of type **10** *via* **6**–**9**. The reverse relative con-

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