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FRAGMENTATION OF ESTER-STABILIZED AMMONIUM YLIDS TO ALKENES

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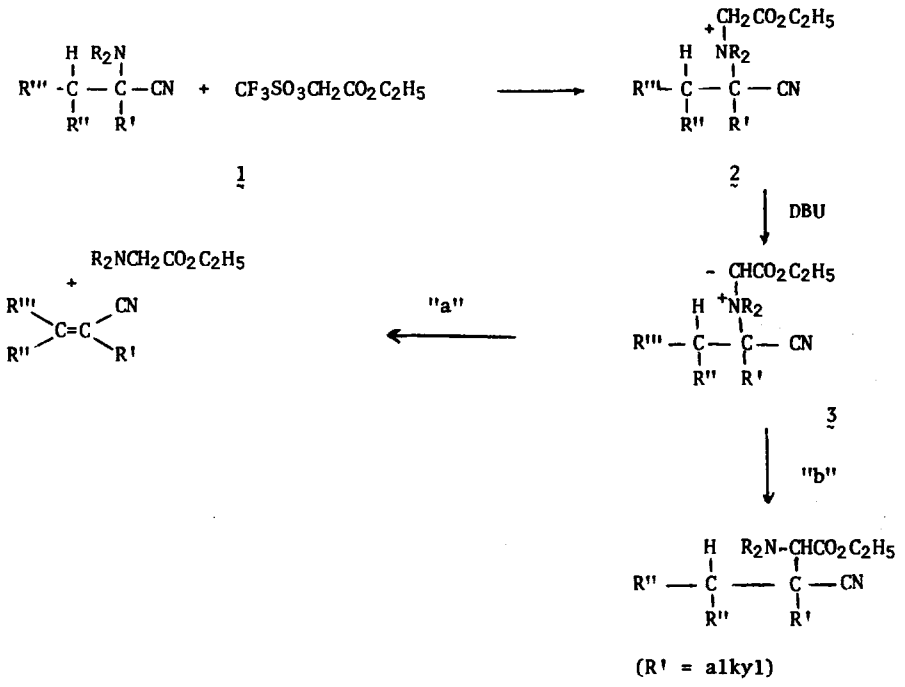
We have recently described a mild procedure for the conversion of sulfides into alkenes by the thermal (typically, room temperature ±30°) elimination of the corresponding ester-stabilized sulfonium ylids.[1] In this communication, we wish to report that analogous elimination of ester-stabilized ammonium ylids is also feasible. A series of α-N,N-dimethylamino nitriles has been alkylated with the trifluoromethanesulfonate ester 1 of ethyl glycolate to give ammonium salts 2. Upon addition of DBU (1,5-diazabicyclo[5.4.0]-undec-5-ene), the salts are converted into ylids 3 which undergo spontaneous fragmentation to alkenes (path "a", Scheme 1).

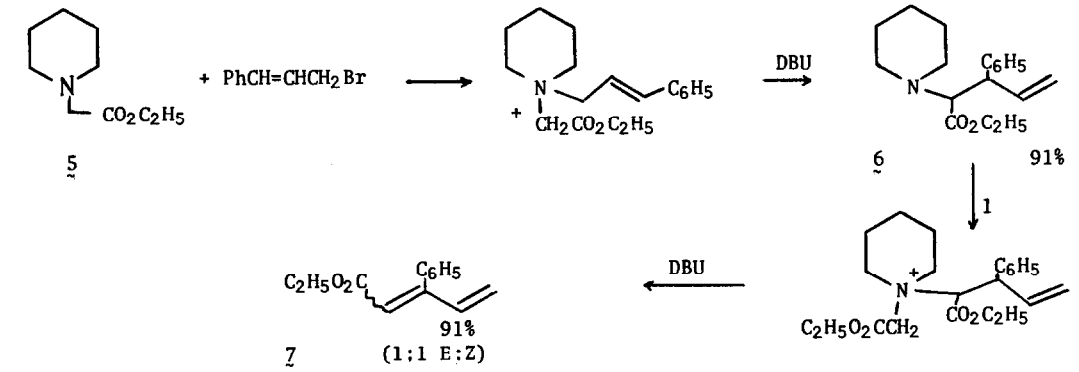
Scheme 1

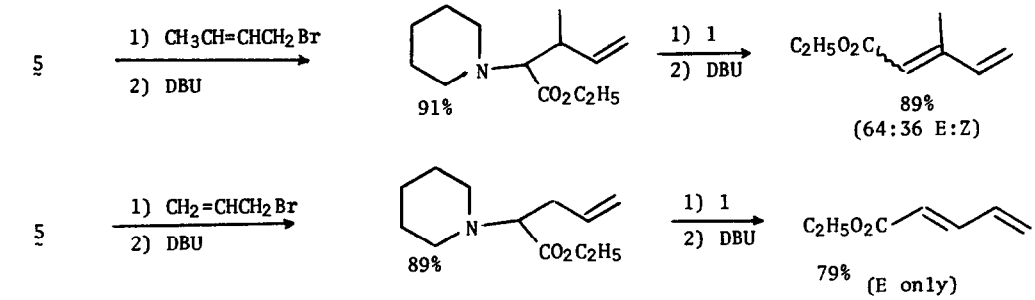


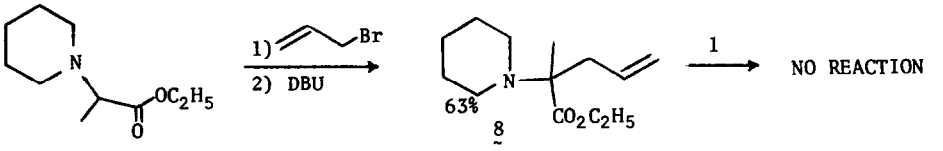
In general, good yields of β-substituted α,β-unsaturated nitriles can be obtained by performing the elimination reaction at 0°. However, the generation of ylids derived from aminonitriles having an additional α-substituent (entries 4 and 6, Table 1) at 0° results in predominant Stevens rearrangement (Scheme 1, path "b"). We have found that this undesired competing reaction can be minimized by adding the ammonium salt to a small excess of DBU in

acetonitrile at -22° (entries 5 and 7).[2] The fragmentation of ylids to α,β-unsaturated nitriles (path "a") is rapid at even lower temperatures. For example, formation of 2-octenonitrile (entry 2, Table 1) from the precursor ammonium salt is complete within a few minutes after DBU addition at -36°. However, an activating substituent at the amine α-carbon such as cyanide or carbonyl is essential for facile elimination. Thus, DBU treatment of salts derived from triflate 1 and simple alkyl amines $RCH_2CH_2N(CH_3)_2$ lacking such activating groups does not result in the formation of alkenes, even after several hours at 50° in acetonitrile.

A sequence of 2,3-sigmatropic shift followed by ammonium ylid fragmentation can be used for synthesis of conjugated diene esters. Thus, treatment of the piperidine ester 5 with cinnamyl bromide ; DBU affords the 2,3-sigmatropic shift product 6 (91% overall). Alkylation of 6 with triflate 1 (15 hrs., RT, acetonitrile) followed by DBU treatment at 0° results in the formation of diene ester 7 (91% from 6) as a 1:1 mixture of E,Z isomers. Other conjugated diene esters can be prepared analogously as summarized below.



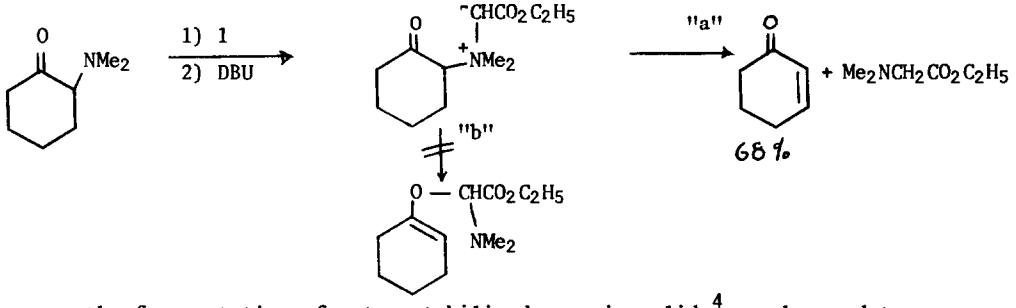




To underscore the utility of triflate 1 for amine alkylations, we note that the hindered and inductively deactivated tertiary amine 6 does not react with ethyl bromoacetate after

several hours at reflux in acetone. However, not even the triflate reagent can alkylate the more hindered amine 8 in acetonitrile solution at a convenient rate.[3]

During our earlier investigation of sulfonium ylid fragmentation, we observed that ylids derived from α-sulfenyl ketones rearrange by an apparent 2,3-sigmatropic shift to form enol ether derivatives.[1] To determine whether this reaction might also operate with ylids prepared from α-amino ketones, we have performed the usual sequence of alkylation and DBU treatment with α-dimethylaminocyclohexanone. In contrast to the behavior of the sulfur analogs, the ammonium ylid undergoes predominant fragmentation to cyclohexenone (path "a"). We can see no evidence to indicate that the "2,3-sigmatropic shift" product (path "b", below) might also be present in the crude product mixture.

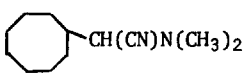
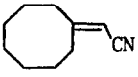
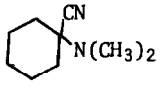
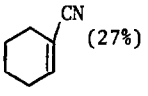
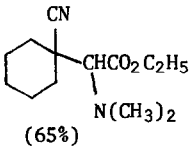
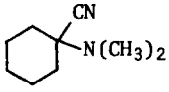
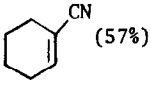
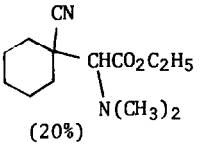


In summary, the fragmentation of ester-stabilized ammonium ylids[4] can be used to prepare α,β-unsaturated esters and nitriles under mild conditions. Yields are typically high, and separation of the conjugated ester or nitrile from the amine byproduct is accomplished readily by amine quaternization with methyl iodide. We have not investigated the details of the fragmentation step, but a 5-center mechanism seems likely by analogy to the behavior of non-stabilized ammonium ylids.[5]

Acknowledgement. This work was supported by the National Institutes of Health (CA17918-02)

1. E. Vedejs and D. A. Engler, Tetrahedron Lett., 3487 (1976).
2. For related examples of temperature-dependent Stevens rearrangement in the sulfur ylid series, see J. E. Baldwin and R. E. Hackler, J. Am. Chem. Soc. 91, 3646 (1969); V. Rautenstrauch, Chem. Commun. 4 (1970).
3. The triflate 1 alkylates acetonitrile at a significant rate at 38° (half life ca. 3 hrs.). Thus, the temperature for alkylation is effectively restricted to 25°. This limitation is not a problem in solvents such as $CHCl_3$, but the alkylation rate is slower in the less polar solvent (ca. 3 x).
4. This reaction has apparently been observed before in the course of ethyl diazoacetate decomposition in triethylamine: V. Franzen and H. Kuntzl, Justus Liebigs Ann. Chem. 627, 15 (1959). However, there can be no comparison in terms of yield or convenience with the triflate; DBU procedure.
5. G. Wittig and R. Polster, Justus Liebigs Ann. Chem. 612, 102 (1957); R. D. Bach, K. W. Bair, and D. Andrzejewski, J. Am. Chem. Soc. 94, 8608 (1972).

TABLE I

ENTRY	STARTING AMINE	TIME FOR ALKYLATION WITH 1 (isol. yield)	TEMPERATURE FOR DBU TREATMENT	PRODUCTS
1)	$C_6H_5CH(CH_3)CH(CN)N(CH_3)_2$	48 hrs. (80%)	0°C	$C_6H_5C(CH_3)=CHCN$ (95%)
2)	$C_6H_{13}CH(CN)N(CH_3)_2$	30 min. (83%)	0°C	$C_5H_{11}CH=CHCN$ (73%)
3)		10 hrs. (100%)	0°C	 (90%)
4)		20 min. (92%)	0°C	 (27%)  (65%)
5)		20 min. (92%)	-22°	 (57%)  (20%)
6)	$C_6H_5CH_2CH_2C(CH_3)(N(CH_3)_2)CN$	24 hrs. (51%)	0°C	$C_6H_5CH_2CH_2C(CN)=CH_2$ (14%) $C_6H_5CH_2CH=C(CH_3)CN$ (8%, E+Z) $C_6H_5CH_2CH_2C(CN)(CH_3)CH(CO_2C_2H_5)N(CH_3)_2$ (65%)
7)	$C_6H_5CH_2CH_2C(CH_3)(N(CH_3)_2)CN$	24 hrs. (51%)	-22°	$C_6H_5CH_2CH_2C(CN)=CH_2$ (38%) $C_6H_5CH_2CH=C(CH_3)CN$ (21%) $C_6H_5CH_2CH_2C(CN)(CH_3)CH(CO_2C_2H_5)N(CH_3)_2$ (17%)

All alkylations with triflate 1 are performed in acetonitrile; ammonium salt yields refer to isolated crystalline product and are not optimized. Ylid fragmentation is performed using 1.1 equivalents of DBU in acetonitrile solution.