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MOLYBDENUM CATALYZED ELIMINATIONS OF ALLYLIC ACETATES. NEW DIENE SYNTHESIS

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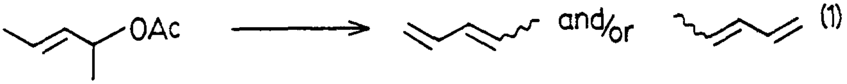
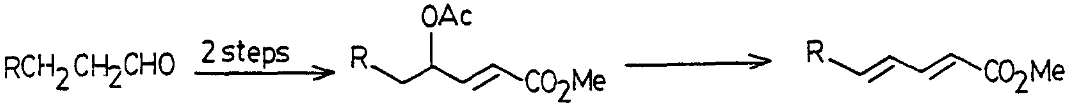
SUMMARY: Allyl acetates smoothly eliminate the elements of acetic acid in the presence of O,N-bis(trimethylsilyl)acetamide and molybdenum hexacarbonyl; a simple sequence permits elaboration of saturated aldehydes into α,β,γ,δ-dienoates which resulted in a four step synthesis of trichonine.

Activation of allylic carboxylates by molybdenum catalysts in the presence of nucleophiles leads to allylic alkylation.[1] Performing such reactions in the absence of nucleophiles has the potential of effecting eliminations to dienes under very mild conditions.[2] The low cost and ease of handling molybdenum catalysts combined with the prospect of regio- and/or stereocontrol led us to examine such a possibility. In this letter, we wish to record the successful realization of this reaction (eq 1) which, combined with a two step synthesis of γ-acetoxy-α,β-unsaturated esters from saturated aldehydes led to a simple strategy to dienoates (eq 2).



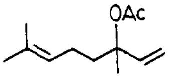
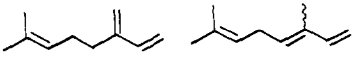
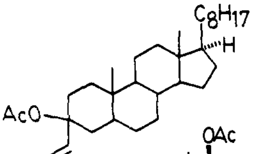
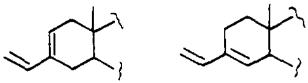
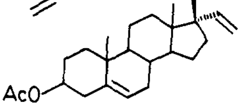
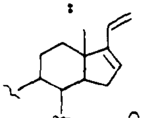
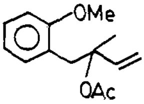
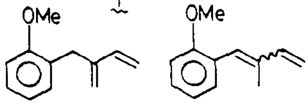
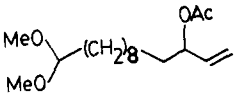
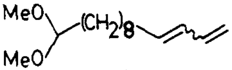
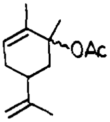
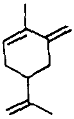
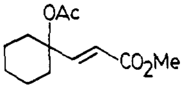
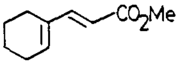
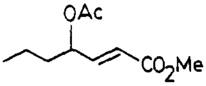
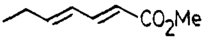
(1)



(2)

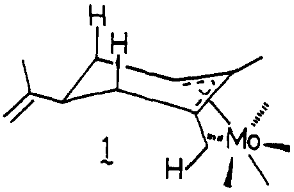
The table summarizes the results. The reaction is performed by heating a toluene solution of the allylic acetate and O,N-bis(trimethylsilyl)acetamide (BSA) with 15 mol% of molybdenum hexacarbonyl (Mo-c). The reaction time depends upon the olefin substituents (alkyl substituents retard but electron withdrawing substituents accelerate) and the substitution on the carbon bearing the carboxylate (rate increases in the order primary < secondary < tertiary). The effects of olefin substitution derive from 1) steric hindrance to form the requisite olefin - molybdenum(O) complex and 2) the energy of the LUMO of the olefin which reflects its ability to participate in back bonding in the initial complex. The trend with respect to the substitution of the allylic carbon seems to derive from a S_N1 component in the transition state for ionization.

TABLE. Diene Synthesis

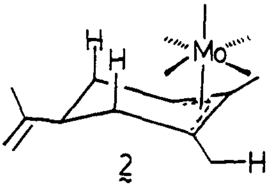
Entry	Substrate	Time	Products	Yield[a]
1		1 h	 45 : 55	75%[b]
2		1.5 h	 2 : 1	85%
3		2 h		67%
4		2.5 h	 20 : 80 (E:Z=7:2)	70%
5		4 h	 E:Z=6:1	45%(50%)
6	 AcO α : β = 1:4	20 h		71%[c]
7		45 min		95%
8		1.5 h	 E,E:E,Z=5:1	68%

(a) All yields refer to pure isolated compounds which gave satisfactory spectral and analytical data. (b) No solvent used. (c) Also recovered was 15% starting material as a 4:1 mixture of α:β acetate isomers.

The reaction is most useful in those cases where the elimination is unidirectional (entries 3,5,7, and 8). The case of the carvone derivative in entry 6 is most unusual; a single diene regioisomer,[3] which is independent of the stereochemistry of the starting acetate, results. Assuming loss of a proton syn to Mo,[4] to the extent that the intermediate corresponds to 1, the only protons



1

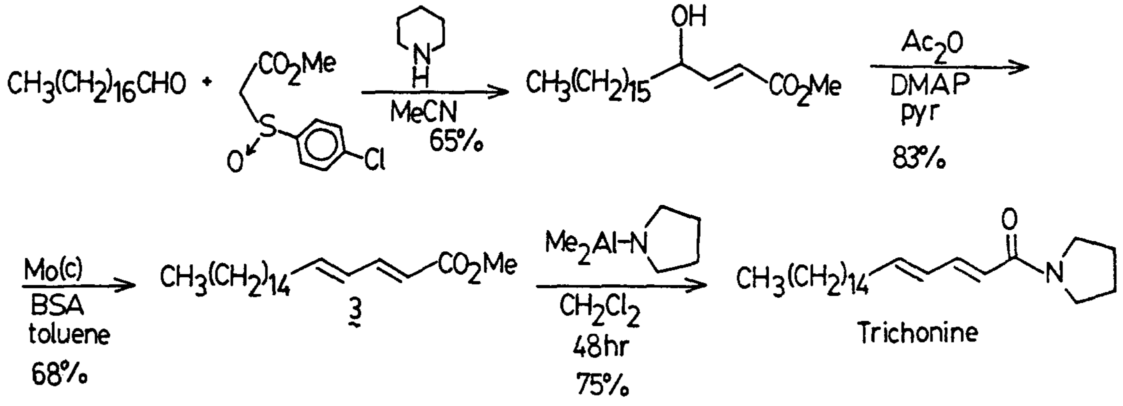


2

properly aligned for elimination are on the methyl group; but, both the ring and methyl protons of isomer 2 are so situated. In this latter case, the diminished steric interactions between the resultant diene and the molybdenum template by forming the exocyclic olefin may account for it too leading to the same diene.[4] Thus, unusual and useful regioselectivity in eliminations indeed results from the use of molybdenum templates.

Such a simple and selective elimination reaction offers a practical approach to natural products possessing polyenes. Polyene carboxamides have a range of interesting biological activity.[5] Combining the very simple conversion of aldehydes to γ-acetoxy-α,β-unsaturated esters by the two step sequence 1) condensation of methyl phenylsulfinylacetate with the saturated aldehyde in the presence of piperidine in acetonitrile at rt or reflux[6,7] and 2) acetylation, with molybdenum catalyzed elimination offers a very efficient approach to such natural products. The starting acetates of entries 7 and 8 were prepared in two steps as outlined above from cyclohexanecarboxaldehyde and pentanal in 66 and 61% yields respectively. Combined with their subsequent elimination, the sequence constitutes a dienoate synthesis according to eq 2. The Scheme illustrates a 4 step synthesis of trichonine from octadecanal (stearyl aldehyde). Elimination produces 3 as a 4:1 E,E:E,Z mixture which, after direct amination using group transfer[8] and recrystallization from hexane gave a 12:1 E,E:E,Z diene ratio, mp 62.5-64° (lit[9] mp 65-7°). Conversion of the ester 3 into its isobutylamide would produce a constituent of the fruit of Piper guineese.[10]

SCHEME. Synthesis of Trichonine



Molybdenum templates are excellent catalysts for eliminations and provide a simple and practical approach for the synthesis of dienes. While the full range of regioselectivity possible remains undefined, the examples show that some unexpected and synthetically useful control can be exercised. Most practical is the strategy for forming dienoates from saturated aldehydes.

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References and Notes

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3. Dehydration of the alcohol by classical methods produces a mixture of all dienes. Jurgen, H.; Schumacher, M.G. *Chem. Ber*. **1959**, **92**, 178; for an alternative approach by epoxide deoxygenation see: Suzuki, H.; Fuchita, T.; Iwasa, A.; Mishina, T. *Synthesis*, **1978**, 905.

4. If an *anti* proton is lost, it would suggest that **2** rather than **1** is the product determining isomer. The unfavorability of the Mo template to occupy a pseudoaxial compared to a pseudoequatorial plane makes such a suggestion less likely. See Faller, J.W.; Murray, H.H.; White, I.L.; Chao, K.H. *Organometllics*, **1983**, **2**, 400.

5. Cf. Bohlmann, F.; Ganzer, M.; Kruger, M.; Nordhoff, E. *Tetrahedron*, **1983**, **3**, 123.

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7. For an alternative multistep approach see De Lombaert, S.; Lesur, B.; Ghosez, L. *Tetrahedron Lett*. **1982**, **23**, 4251.

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11. The following procedure is representative (entry 7). To a flask containing dry toluene (1 ml) was added sequentially 134 mg (0.66 mmol) of O,N-bistrimethylsilylacetamide then 100 mg (0.44 mmol) of the acetate. This mixture was heated at 110° for 10 min, cooled, then 17 mg (15 mol%) $Mo(CO)_6$ added and the mixture refluxed for 0.75 h. The crude reaction was added directly to a flash column and eluted (4:1 hexane:ether) to yield 70 mg (95%) of the diene as a clear oil.

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