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VINYLOGOUS DIECKMANN CONDENSATION:
AN APPLICATION OF BALDWIN'S RULES.

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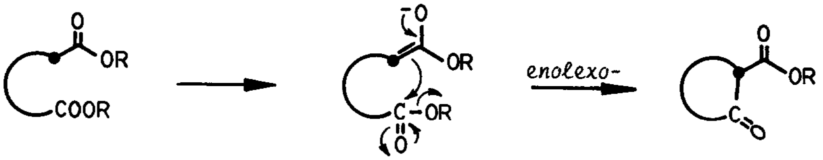
ABSTRACT: Vinylogous Dieckmann condensations equivalent to enolexo-exo-trig and enolendo-exo-trig cyclisations have been investigated. Five membered rings were smoothly obtained from the former whereas the latter cyclisations occurred with six but not with five membered ring systems.

The Dieckmann condensation (equation i) has recently been described by Baldwin as an n-(enolexo)-exo-trig cyclisation, and a "*favoured process*".[1,2] However, cyclisations such as that depicted in equation ii have been concluded, independently by both House[3] and Baldwin[4], to be of the enolendo type, and is dependent on the value of n. Accordingly, a base catalysed cyclisation of 5-halo-2-pentanone would be difficult, and the reaction is described as a "*disfavoured process*".



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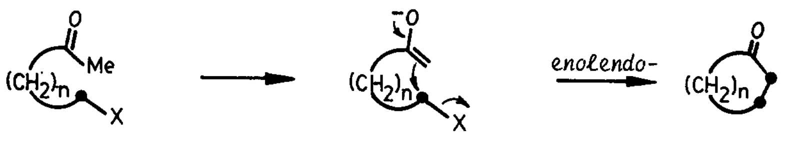
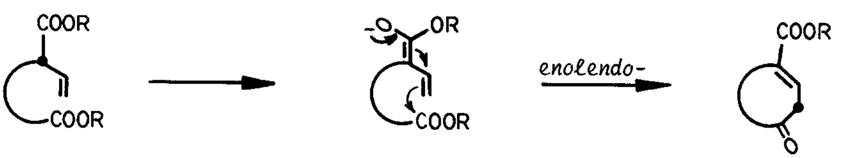


·······(ii)

There is no report on whether or not these concepts can be extended to conjugated enolate systems, and we now wish to present two types of vinylogous Dieckmann condensations (equations iii and iv) which are, in fact, extended enolendo and enolexo cyclisations respectively.



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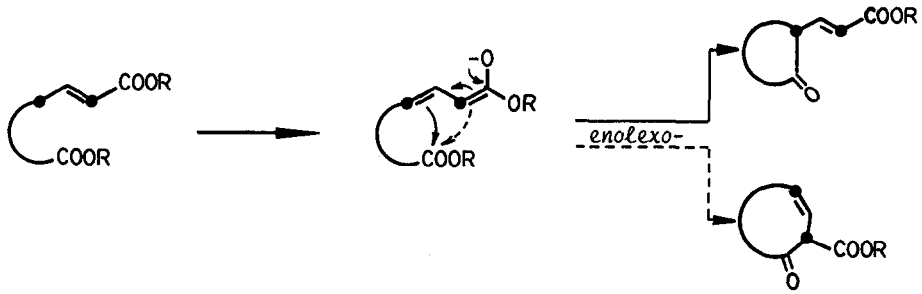
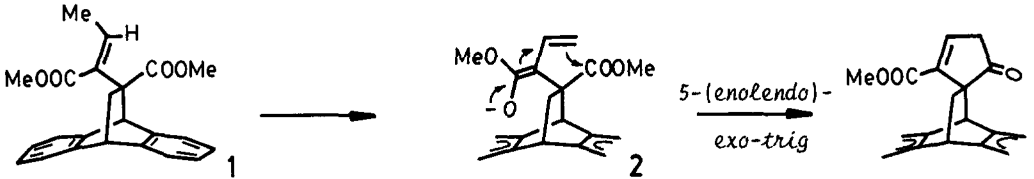


...... (iv)

During the course of our work on the synthesis of cyclopentenoid antibiotics[5] we attempted the cyclisation of compound 1 with the aim of obtaining the valuable precursor 3. However, no trace of 3 could be detected when 1 was subjected to the standard cyclisation conditions (LDA, THF/TMEDA, -78° then room temp. for 8 hr)[6], and we obtained, instead, the starting material 1 together with 4, 5, and 6 in 12%, 16%, 14%, and 27% purified yields respectively.[7] The stereochemistry of compounds 1 and 4 were assigned from their nmr spectra (1: δ 1.70, Me; 5.98, vinylic H. 4: δ 1.65, Me; 6.22, vinylic H) but no attempt was made to distinguish between 5 and 6, hence the stereochemistry shown is arbitrary and the yields of 14% and 27% could well be reversed.



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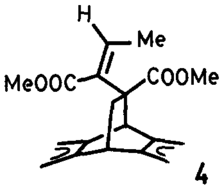

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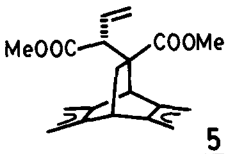

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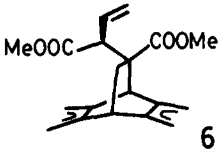

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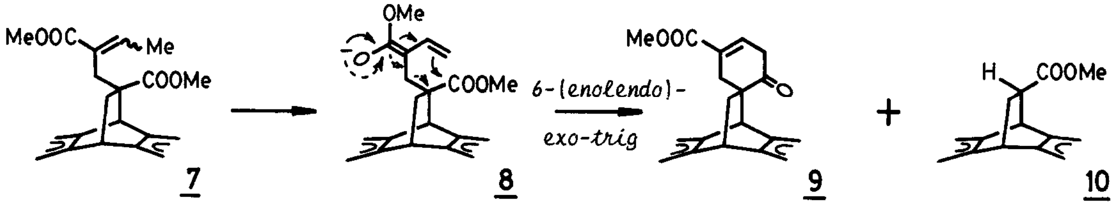
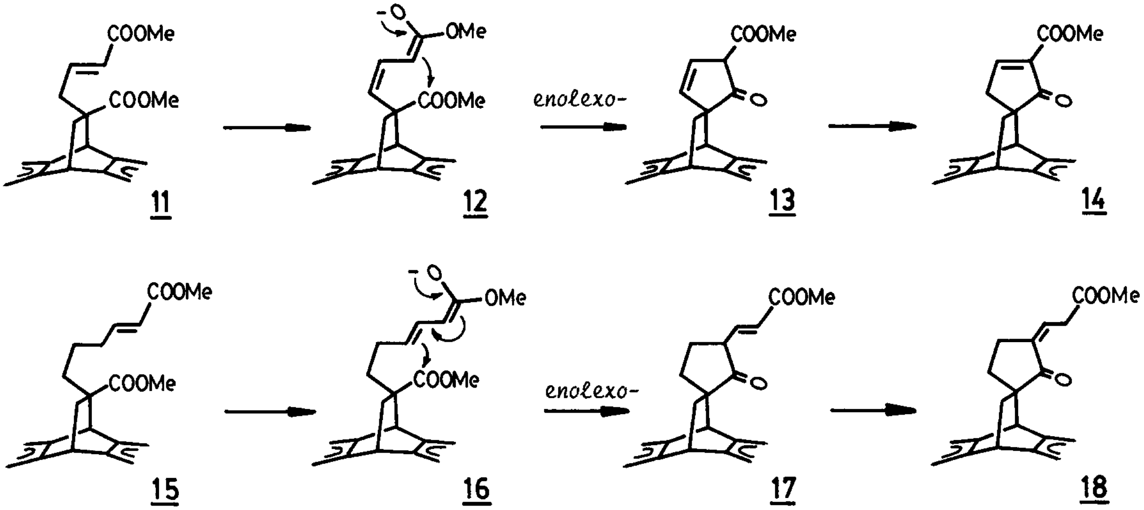
The presence of isomeric 1, 4, 5, and 6 is strong indication that the dienolate 2 was indeed formed but failed to cyclise in a 5-(enolendo)-exo-trig fashion, which process has already been described as "*disfavoured*".[8]

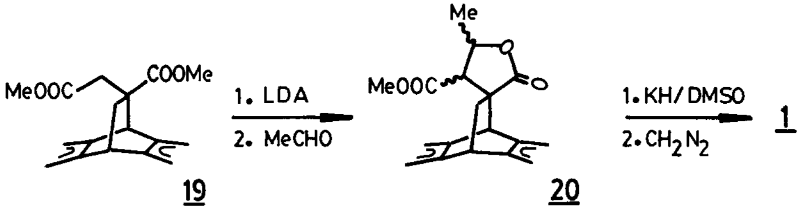
A 6-(enolendo)-exo-trig cyclisation, on the contrary, is known to be a "*favoured process*"[2] and we therefore subjected the diester 7, the homologue of 1, to the same reaction conditions and were tantalized to find that this conjugated system did indeed cyclise to give 9 (64%). A certain amount (21%) of adduct 10, probably resulting from a retro Michael addition of the dienolate 8, was also isolated from this reaction.



Having differentiated between the vinylogous 5- and 6-(enolendo)-exo-trig cyclisations we then turned our attention to the vinylogous enolexo process as outlined in equation iv. Here compounds 11 and 15 were employed[9] and, as expected, both cyclised in a manner equivalent to a 5-(enolexo)-exo-trig process followed by double bond isomerisations to yield 14 (43%) and 18 (54%) respectively. It should be noted that the dienolate 16 could, in fact, adjust to a suitable geometry for a 7-(enolexo)-exo-trig cyclisation to form a cycloheptenone ring but such a reaction was not observed and the reaction gave only 18.



Preparation of the starting material 1 deserves some comments. Treatment of the enolate from the itaconate-anthracene adduct 19 with acetaldehyde yielded the lactone 20 as a mixture of two separable isomers in a ratio of 6.5 : 1 (75%). Base catalysed (KH/DMSO, room temp.) ring opening reaction of the major isomer gave an acid which upon methylation (CH_2N_2) yielded pure 1 (72%).[10] This overall process is, in fact, the well known Stobbe condensation.



Interestingly, a recent attempt at a very similar ring opening reaction was reported to be unsuccessful, and the authors regarded the failure of the reaction as due to a disfavoured "retro-5-endo-trigonal cyclisation".[11]

To conclude, the vinylogous Dieckmann condensation of the various systems described here have all been found to strictly obey Baldwin's rules. It is, therefore, good precaution that the rules be given consideration when synthetic strategies are being planned. Certainly, the rules should not be regarded as ***BALDWIN'S FOLLY.***"

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4. J.E.Baldwin, L.I.Kruse, J.Chem.Soc.Chem.Comm., 1977, 233.
5. Examples are ; SARKOMYCIN (H.Umezawa, T.Takeuchi, K.Nitta, Y.Yamamoto, S.Yamaoka, J.Antibiot., 1953, 6, 101), METHYLENOMYCIN A (T.Haneishi, N.Kitihara, Y.Takiguchi, M.Arai, S.Sugawara, J.Antibiot., 1974, 27, 386), DEEPOXY-4,5-DIDEHYDROMETHYLENOMYCIN A (U.Hornemann, D.A.Hopwood, Tetrahedron Lett., 1978, 2977).
6. T.Siwapinyoyos, Y.Thebtaranonth, J.Org.Chem., 1982, 47, 598.
7. All products described here gave satisfactory physical data.
8. Very recently a cyclisation similar to the 5-(enolendo)-exo-trig process has been reported (R.Danieli, G.Martelli, G.Spunta, S.Rossini, G.Cainelli, M.Panunzio, J.Org.Chem., 1983, 48, 123). However, there are marked differences between 1 and the reported system, including the reaction conditions employed.
9. 15 was prepared by alkylation of the adduct 10 with methyl 6-bromocrotonate followed by introduction of the double bond, while 11 was obtained from our previous work (P.Prempree, S.Radviroongit, Y.Thebtaranonth, J.Org.Chem., 1983 48, 3553).
10. 7 (single compound, stereochemistry not known) was prepared in a similar manner starting from 10.
11. R.M.Scarborough, Jr., B.H.Toder, A.B.Smith, III, J.Amer.Chem.Soc., 1980, 102, 3904. Compare with ref. 8.
12. *"The rules that I have enunciated for ring closure which some have called Baldwin's rules may also be Baldwin's folly"*, quotation taken from "Further Perspectives in Organic Chemistry", Ciba Foundation Symposium 53, Elsevier/Excerpta Medica/North Holland, 1979, p. 85.

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