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NEW YLIDE ANIONS.
A VINYL ANION EQUIVALENT FOR SUBSTITUTED FUMARATE ESTERS

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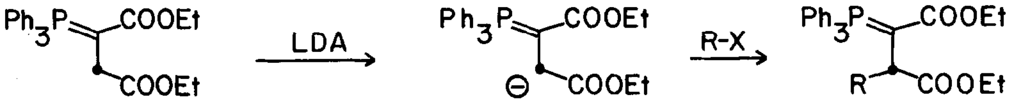
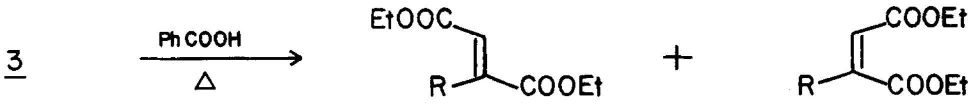
ABSTRACT: A new type of ylide anion is reported which upon alkylation and elimination of triphenylphosphine serves as a vinyl anion equivalent.

We wish to report a new approach to vinyl anion equivalents made possible by the facile formation of a new type of ylide anion.[1] Deprotonation of 1, readily obtained from the addition of triphenylphosphine to diethyl fumarate,[2] with LDA in THF at -78° rapidly gives a dark orange solution of ylide anion 2. This anion is formally analogous to the recently reported 1,2-dicarboxylate dianions.[3] Ylide anion 2 is readily alkylated by ordinary halides at 0° giving good yields of the substituted ylide 3 which may be purified by chromatography (silica gel, EtOAc-MeOH, 9:1). Results of typical alkylations are shown in the Table.



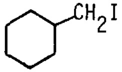
1 2 3

Regeneration of the olefinic link requires removal of the elements of triphenylphosphine. While such extrusions have been reported to occur at around 170° in related systems,[4] a milder method was sought. Following the lead of Bestman[5] in work with related keto-ylides, we have found that the removal of triphenylphosphine is readily accomplished upon heating 3 in refluxing toluene in the presence of a catalytic

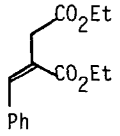


4 5

TABLE. Ylide anion 2 as a vinyl anion equivalent.

Entry	RX	Yield 3[a] (%)	mp 3	Yield % 4+5	4:5[b]	Yield 4 isolated (%)	mp Diacid from 4	Lit. mp
1	CH_3I	89	168-170°	100[c]	83:17	--	d	
2	n-PrI	92	131-133°	99[c]	75:25	--	173-173.5°	173-174°[10]
3		72	131-133°	96[c]	72:28	65	204.5-206°	204.5-206°[9]
4	n-BuBr	93	130-132°	--	74:26	70	167-168°	169-170°[10]
5	$PhCH_2CH_2Br$	84	118-120°	--	75:25	68	196-199.5°	198.5-200°[9]
6	$PhCH_2Br$	95	148-153°	f	--	52	g	--
7	i-PrI	66	155-157°	92[c]	35:65	--	183-186°	185-186°[10]
8	n-$C_{10}H_{21}I$	--	--	84[e]	72:28	61	--	--

[a] Satisfactory analytical data was obtained for all crystalline products. [b] Determined by glc or H nmr analysis.[7] [c] Glc analysis. [d] Esters identified by comparison with authentic samples. [e] Isolated. [f] Olefins consisted of 52% 4 and 45%



. [g] Both esters characterized through spectra and C,H analysis.

amount of benzoic acid. While the origin of the stereochemical outcome is not yet clear,[6] E-isomer formation predominates in most cases as seen in the Table.[7] This predominance combined with facile isomer separation[8] make ylide anion 3 a synthetically useful source of a vinyl anion equivalent in the preparation of substituted fumarate esters which are not conveniently prepared by present literature methods.[9,10] A typical procedure is given.

Diethyl n-decylfumarate (4, R=n-$C_{10}H_{21}$). A solution containing 12 mmol of LDA in 50 ml of the THF (from 12 mmol of i-Pr_2NH and 11 mmol of 1.56N n-butyllithium in hexane at -78°) was stirred under argon at -78° while a solution containing 10 mmol of 1 in 20 ml of THF was added dropwise over 2 min. The resulting dark orange solution was stirred at -78° for 15 min. and treated with 12 mmol of n-decyl iodide. The solution was stirred at 0° for several hours and then allowed to warm to room temperature overnight. Solvent was removed under reduced pressure and the residue extracted with methylene chloride - water. The oil obtained after solvent removal was placed in 40 ml of toluene containing 700 mg benzoic acid and heated at reflux for 20 hr. Solvent removal followed by pentane-water-$NaHCO_3$ extraction gave a mixture of olefins which was easily separated on a short column of silica gel. Elution with hexane followed by CH_2Cl_2-hexane (1:1) gave 1.91g (61%) of pure diethyl n-decylfumarate, bp 136-138° (0.25 mm); NMR (CCl_4) C=CH δ 6.75; C,H anal.

Treatment of ylide anion 2 with cyclohexanone or butyraldehyde failed to give the desired carbonyl adducts. In both cases the color of 2 was rapidly discharged upon warming to -30° but only starting ylide 1 could be detected (tlc). This suggests that proton abstraction is the dominate reaction with enolizable carbonyl compounds although facile retro-condensation has not been excluded.

We have also investigated the possibility that 2 might be used in ring-forming reactions resulting from alkylations with bifunctional electrophiles and subsequent intramolecular reactions at the less nucleophilic ylide center. Treatment of 2 with excess 1,3-dibromopropane gave an alkylated ylide which upon heating in THF in the presence of N,N-diisopropylethyl amine underwent intramolecular cyclization and elimination to give diethyl cyclopentene-1,2-dicarboxylate in 58% isolated yield. Alkylation of 2 with 1,4-dibromobutane followed by prolonged heating gave no carbocycle and the intermediate alkylated ylide 3 (R = $Br(CH_2)_4$) could be subsequently isolated in 93% yield. The corresponding iodide was likewise resistant to cyclization.

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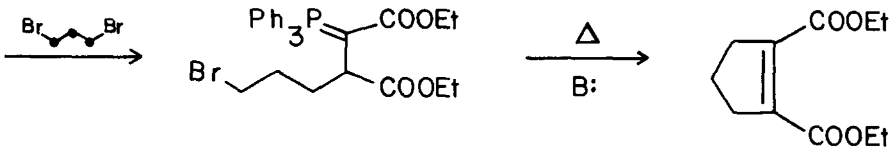
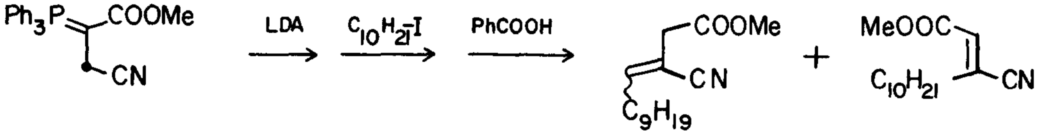


Finally, we have briefly investigated cyano-ylide 6[11] which is readily deprotonated by LDA and was alkylated in 94% yield by n-decyl iodide. Elimination of



6 8 9

triphenylphosphine is notably slower in this case, however, requiring 30 hr of heating with benzoic acid (3 typically requires only 4 hrs) and results in the formation of a major amount of 8 as an equal mixture of geometric isomers and only minor amounts of the expected isomer, 9. The longer reaction time required in the elimination step may encourage isomerization of initially formed 9.

The introduction of other useful structural units as nucleophiles using this approach is under investigation.

Acknowledgment. We thank the National Science Foundation for their support.

References and Notes

1. For a previously reported synthetically useful acyl ylide anion see: M.P. Cooke, Jr., J. Org. Chem., 38, 4082 (1973); J.D. Taylor and J.F. Wolf, J. Chem. Soc., Chem. Commun., 876 (1972).
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6. The isomeric olefins appear to be of kinetic origin in that the E/Z ratio remains unchanged throughout the reaction. Neither 4 nor 5 are isomerized in the presence of triphenylphosphine and benzoic acid. Isomerization and hence rapid equilibration of the two isomers in the presence of the basic ylide precursor 3, or benzoate anion generated in its presence, cannot be excluded.
7. Stereochemistry was determined from vinyl HNMR resonances typically found to be δ 6.8 and 5.8 for E and Z-isomers, respectively, and by hydrolysis of E-isomers to their known diacids. Only in the case containing the bulky iso-propyl group (entry 7) was Z-isomer predominance observed.
8. The olefins and triphenylphosphine were separated by chromatography (silica gel, CH_2Cl_2). Typically, R_F 4=0.60, R_F 5=0.35.
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