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SULFUR YLIDES. COMMUNICATION 1. CYCLOPROPANATION OF α,β-UNSATURATED KETONES WITH ETHYL(DIMETHYL-SULFURANYLIDENE)ACETATE GENERATED IN THE PRESENCE OF PHASE-TRANSFER CATALYSTS

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Stabilization of the sulfur ylide ethyl(dimethylsulfuranylidene)acetate (I) is usually carried out by deprotonation of the sulfonium salt $(CH_3)_2\overset{\oplus}{S}CH_2CO_2EtBr^{\ominus}$ (II) by reaction with NaH in THF [1] or with a mixture of a saturated solution of K_2CO_3 and 12.5 N NaOH solution in chloroform [2]. Although the method for the preparation of (I) is not complicated, cyclopropanation reactions of activated olefins with it do not always proceed satisfactorily.

We have shown that cyclopropanation of α,β-unsaturated ketones at ~20°C in the presence of phase-transfer catalysts proceeds with good yields when (I) is generated in situ from the sulfonium salt (II) and KOH powder (85%) in organic solvents [3]. In selecting the optimal reaction conditions for the cyclopropanation we used mesityl oxide (III) as the substrate, which led to the formation of one reaction product (IV) (Table 1).

High yields of the ethyl ester of 2,2-dimethyl-3-acetyl-cyclopropanecarboxylic acid (IV) were obtained by using triethylbenzylammonium chloride (TEBAC) as catalyst and THF as solvent. When no catalyst is present, and also when anhydrous KOH is used, the reaction practically does not take place. By replacing KOH with NaOH, K_2CO_3, or Et_3N product (IV) is formed in low yield. Raising the reaction temperature increases the reaction rate, but the yield of (IV) is lowered due to the formation of by-products.

When the sulfonium salt $(CH_3)_2\overset{\oplus}{S}CH_2CO_2MeBr^{\ominus}$ (V) is used instead of the sulfonium salt (II), the yield of the cyclopropanation product is lowered considerably. Introduction of a furan or benzene substituents raises the electrophilicity of the starting substrate, which is reflected in an increased yield of the product of the cyclopropanization reaction (Table 2). On cyclopropanization of enones with different substituents R^1 and R^2, a mixture of stereoisomers is formed. Their ratios vary within a wide range, generally with predominance of

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TABLE 1. Cyclopropanation of Mesityl Oxide

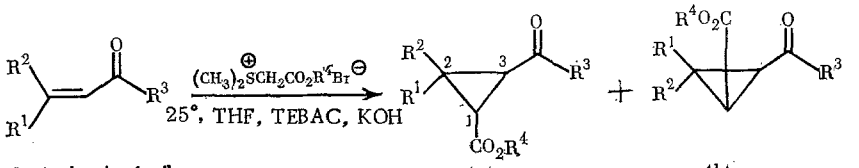
Base	Catalyst*	Solvent	Reaction temp., °C	Time, h	Yield, %
KOH	TEBAC	THF	25	1,5	73
KOH	TBAI	THF	25	5	34
KOH	TBAB	THF	25	5	20
KOH	—	THF	25	5	8
KOH	TEBAC	CH_2Cl_2	25	5	2
KOH	TEBAC	$CHCl_3$	25	5	0
KOH	TEBAC	C_6H_6	25	5	32
KOH	TEBAC	DMSO	25	5	0
KOH	TEBAC	1,4-Dioxane	25	5	2
KOH	TEBAC	Monoglyme	25	5	38
KOH (pellets)	TEBAC	THF	25	5	0
KOH	TEBAC	THF	66	0,2	18
NaOH (pellets)	TEBAC	THF	25	5	4
NaOH (85%)	TEBAC	THF	25	5	2
NaOH (pellets)	TBAI	THF	25	5	0
12,5 *N* solution of NaOH + + sat. solution of K_2CO_3	TBAI	CH_2Cl_2	40	30	30
12,5 *N* NaOH + solution of K_2CO_3	TEBAC	CH_2Cl_2	40	24	3
Solution of NaOH	TEBAC	CH_2Cl_2	40	3	20
Solution of K_2CO_3	TEBAC	$CHCl_3$	25	20	0
Et_3N	—	THF	25	20	2

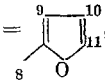
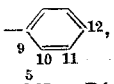
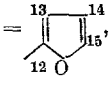
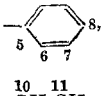
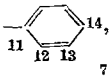
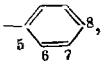
*TEBAC: triethylbenzylammonium chloride; TBAI: tetrabutylammonium iodide; TBAB: tetrabutylammonium bromide.

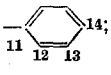
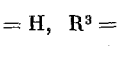
TABLE 2. Cyclopropanation of Enones

Starting enone	Reaction products	Yield, %	Ratio of isomers (a):(b)	Starting enone	Reaction products	Yield, %	Ratio of isomer (a):(b)
(III)	(IV)	73	100 : 0	(VIII)	(XV)	65	26 : 74
(III)	(VI)	30	100 : 0	(IX)	(XVI)	96	96 : 4
(VII)	(XII)	93	70 : 30	(X)	(XVII)	89	62 : 38
(VII)	(XIII)	48	67 : 33	(XI)	(XVIII)	50	72 : 28
(VIII)	(XIV)	77	39 : 61				

isomer (a), which is characterized by the trans position of the carbethoxy group and the substituent containing the carbonyl group.



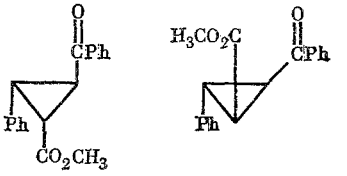
$R^1 = R^2 = R^3 = CH_3$ (III), R^1 = α-furyl, $R^2 = H$, $R^3 = CH_3$ (VII); $R^1 = Ph$, $R^2 = H$, $R^3 = CH_3$ (VIII); R^1 = α-furyl, $R^2 = H$, $R^3 = Ph$ (IX); $R^1 = Ph$, $R^2 = H$, $R^3 = Ph$ (X); $R^1 = Ph$, $R^2 = H$, R^3-cyclopropyl (XI); $R^1 = \overset{10}{C}H_3$, $R^2 = \overset{9}{C}H_3$, $R^3 = \overset{5}{C}H_3$, $R^4 = \overset{7}{C}H_2\overset{8}{C}H_3$ (IV); $R^1 = \overset{9}{C}H_3$, $R^2 = \overset{8}{C}H_3$, $R^3 = \overset{5}{C}H_3$, $R^4 = \overset{7}{C}H_3$ (VI); $R^1 =$  , $R^2 = H$, $R^3 = \overset{5}{C}H_3$, $R^4 = \overset{7}{C}H_2\overset{8}{C}H_3$ (XII); $R^1 =$  , $R^2 = H$, $R^3 = \overset{5}{C}H_3$, $R^4 = \overset{7}{C}H_3$ (XIII); $R^1 =$  , $R^2 = H$, $R^3 = \overset{5}{C}H_3$, $R^4 = \overset{7}{C}H_2\overset{8}{C}H_3$ (XIV); $R^1 =$  , $R^2 = H$, $R^3 = \overset{5}{C}H_3$, $R^4 = \overset{7}{C}H_3$ (XV); $R^1 =$  , $R^2 = H$, $R^3 =$  , $R^4 = \overset{10}{C}H_2\overset{11}{C}H_3$ (XVI); $R^1 =$  , $R^2 = H$, $R^3 =$  , $R^4 = \overset{10}{C}H_2\overset{11}{C}H_3$ (XVII):

$R^1 =$  ; $R^2 = H$, $R^3 =$  ; $R^4 = \overset{9}{C}H_2\overset{10}{C}H_3$ (XVIII).

Isomers (XIVa) and (XVIb) and (XVa) and (XVb) were separated by means of preparative GLC. Other isomers, (XIIa) and (XIIb) and (XVIIIa) and (XVIIIb), were separated by column chromatography over silica gel. Comparative experiments on the cyclopropanation of all enones with previously prepared (I) (benzenes, 18-27 h, 80°C) demonstrated complete identity of the ratios of the cis and trans isomers.

Thus, the stereochemistry of the starting compound (I), prepared in situ from the sulfonium salt, does not differ from that obtained when previously prepared ylide is used.

The structure of the isomers was assigned on the basis of ^1H and ^{13}C NMR spectroscopic data. The configurations of the substituents at the atoms C^1 and C^3 of the compounds (IV) and (VI) were unambiguously established by analyzing the chemical shifts of the carbon atoms of the methyl groups C^9 and C^{10} (IV) and C^8 and C^9 (VI). For each methyl group the existence of the cis interaction led to a minor difference in the signals of the methyl groups of up to 1 ppm, which suffices for assigning compounds (IV) and (VI) to the trans series [4]. Up to now, for compounds having only one substituent on each carbon atom of the cyclopropane ring, we do not have accurate criteria which make it possible to carry out stereochemical analyses based on ^1H and ^{13}C NMR spectroscopic data. Adams et al. [5] have analyzed the PMR spectra of the isomer pair



However, the presence in each isomer of two $^3J^{HH}_{cis}$ and one $^3J^{HH}_{trans}$ vicinal constants, which differ only slightly (4.5 and 5, 6.5 and 7; 10 and 10 Hz), makes unambiguous assignment of stereochemistry on the basis of PMR spectra difficult. The values of the chemical shifts of the proton signals of the isomer pair also differ insignificantly.

The chemical shifts of the carbon atoms of the cyclopropane rings of the isomer pairs are close together in the ^{13}C NMR spectra, which makes the assignment of the signals of C^2 and C^3 and the stereochemical assignment of each isomer to the cis and the trans series difficult. The signals of the carbon atoms that are in the α-position of the cyclopropane ring provide much information. It can be seen in Table 3 that the signals of the carboxyl carbon atoms differ not more than 0.65 ppm in the isomer pairs. This fact points to the absence of the two other possible isomers with the 1,2- and 1,3-trans-trans and the 1,2- and 1,3-cis-cis position of the substituents because in those cases the carbon atom of the carbozyl group would undergo a quite different type of interaction causing a great difference in chemical shift. Moreover, the trans configuration of the substituents at C^2 and C^3 follows from the trans configuration of the starting enone. The configuration of the substituents at C^2 and C^3 remains constant in the series (a) and (b) and therefore from here on it was of interest to establish the configuration of the substituents at C^1 and C^3, while series (a) was attributed to compounds having trans position of the substituents and series (b) to compounds having cis position of the substituents. The assignment of the isomers to the cis or the trans series was performed on the basis of the relationship of the signals of the carbon atoms that are in α-position to the atoms C^1 and C^3 of the cyclopropane ring. The diamagnetic shift of the C^3 signal of up to 3 ppm and the paramagnetic shift of the carbonyl atom C^4 of up to 4 ppm relative to the corresponding signals of the isomer pair is evidence of the affiliation of compound (XIIa) to the trans series and of compound (XIIb) to the cis series.

The difference in chemical shift of the signals of the isomer pair results from one cis interaction of the carboxyl carbon with different substituents at C^2 and C^3. An analogous relationship of the signals of the carbonyl atom C^4 and the signal of the carbon atom in the α-position to C^2 enables us to assign the isomer pairs (XIV)-(XVIII) unambiguously to the cis and trans series.

EXPERIMENTAL

PMR spectra were taken on a Tesla BS-497 instrument (100 MHz) and ^{13}C NMR spectra on a Jeol FX-900 in $CDCl_3$ with TMS as standard; IR spectra were recorded on a UR-20 apparatus (films). GLC analyses were carried out on a Khrom-5 chromatograph (column: 5% NZhFSE-30 on

TABLE 3. ^{13}C NMR Spectra of the Esters of Cyclopropanecarboxylic Acids (δ, ppm, $CDCl_3$)

Compound	C¹	C²	C³	C⁴	C⁵	C⁶	C⁷	C⁸
(IVa)	34,14 d	32,77 s	41,45 d	203,79 s	31,98 q	170,50 s	60,64 t	14,25 q
(VIa)	33,91 d	32,93 s	41,61 d	203,93 s	32,05 q	171,06 s	51,83 q	20,66 q
(XIIa)	30,68 d	32,83 d *	26,44 d *	203,83 s	30,94 q	168,02 s	60,80 t	14,07 q
(XIIb)	30,42 d	35,22 d *	23,24 d *	200,66 s	29,90 q	167,78 s	60,80 t	14,03 q
(XIVa)	31,76 d	34,53 d *	32,96 d *	204,77 s	31,07 q	168,41 s	60,77 t	13,97 q
(XIVb)	32,05 d	37,86 d *	30,29 d *	202,62 s	30,94 q	169,07 s	61,30 t	14,23 q
(XVa)	31,59 d	34,66 d *	33,19 d *	204,80 s	31,30 q	168,94 s	51,86 q	134,34 s
(XVb)	31,76 d	37,63 d *	30,32 d *	202,55 s	30,81 q	169,39 s	52,22 q	137,77 s
(XVIa)	30,88 d	29,64 d *	29,93 d *	195,79 s	136,79 s	128,43 d	128,76 d	133,59 d
(XVIb)	30,03 d	32,96 d *	23,14 d *	193,26 s	133,33 s	128,43 d	128,76 d	133,59 d
(XVIIa)	29,51 d	34,89 d *	32,08 d *	196,31 s	138,16 s	128,27 d	128,69 d	133,39 s
(XVIIb)	29,58 d	35,05 d *	31,66 d *	193,41 s	138,03 s	128,27 d	128,64 d	132,69 d
(XVIIIa)	31,76 d	34,50 d *	32,70 d *	206,99 s	21,77 d	11,45 t	11,55 t	168,51 s
(XVIIIb)	31,99 d	37,76 d *	29,89 d *	202,88 s	21,97 d	10,90 t	11,16 t	168,77 s

Compound	C⁹	C¹⁰	C¹¹	C¹²	C¹³	C¹⁴	C¹⁵
(IVa)	20,63 q	19,71 q					
(VIa)	19,68 q						
(XIIa)	148,09 s	107,97 d	110,51 d	141,78 d			
(XIIb)	150,82 s	106,27 d	110,48 d	140,90 d			
(XIVa)	134,47 s	128,07 d	128,96 d	127,22 d			
(XIVb)	138,00 s	126,51 d	128,72 d	127,22 d			
(XVa)	128,17 d	128,63 d	127,29 d				
(XVb)	126,32 d	128,63 d	127,12 d				
(XVIa)	168,41 s	61,13 t	14,10 q	149,19 s	108,00 d	110,54 d	141,78 d
(XVIb)	168,41 s	61,13 t	14,10 q	151,13 s	108,00 d	110,54 d	141,42 d
(XVIIa)	168,51 s	60,77 t	14,00 q	134,82 s	128,14 d	128,86 d	127,22 d
(XVIIb)	168,96 s	61,16 t	14,00 q	138,03 s	126,53 d	128,53 d	127,03 d
(XVIIIa)	60,67 t	14,00 q	134,66 s	128,07 d	128,89 d	127,16 d	
(XVIIIb)	61,07 t	14,20 q	138,16 s	126,41 d	128,56 d	126,97 d	

*Possibly reversed assignment of the signals.

Chromaton N-AW-HMDS, column length 1.2 m). Mass spectra were taken on an MX-1306 instrument operating under standard conditions. The preparative separation of isomers was carried out with an LKhP-7I apparatus using the phase 15% PÉG-6000 on Chromaton N-AW; column 0.84 m long with a diameter of 18 mm.

The synthesis of the sulfonium salts (I) and (II) was carried out according to [2] and that of (V) according to [6].

Method of Cyclopropanation of α,β-Unsaturated Ketones. A mixture of 10 mmoles of enone, 10 mmoles of sulfonium salt, 10 mmoles of KOH powder (85%), and 0.15 mmole of TEBAC in 20 ml of THF was stirred for 1-2 h at about 20°C. The precipitate was filtered off, the solvent evaporated, and the residue vacuum distilled.

Ethyl 2,2-dimethyl-3-acetylcyclopropanecarboxylate (IV) was prepared from salt (II) and enone (III), bp 65°C (1 mm), n_D^{25} 1.4555; IR spectrum (ν, cm^{-1}): 1710, 1745 (C=O). PMR spectrum (δ, ppm): 1.44 s (CH_3), 1.07 t (CH_3), 2.22 s ($COCH_3$), 2.23-2.71 m (CH, CH-cyclopropyl), 4.07 q (CO_2CH_2). m/e 184 (M^+).

Methyl 2,2-dimethyl-3-acetylcyclopropanecarboxylate (VI) was prepared from salt (V) and enone (III), bp 56°C (1 mm). IR spectrum (ν, cm^{-1}): 1710, 1745 (C=O). PMR spectrum (δ, ppm): 1.13 s (CH_3), 1.3 s (CH_3), 2.2 s ($COCH_3$), 2.27-258 m (CH, CH-cyclopropyl), 3.6 s (OCH_3). m/e 170 (M^+).

Ethyl 2-(α-furyl)-3-acetylcyclopropanecarboxylate (XIIa,b) was prepared from salt (II) and enone (VII), bp 140°C (1 mm), n_D^{25} 1.4945. IR spectrum (ν, cm^{-1}): 1715, 1740. PMR spectrum (XIIa), (δ, ppm): 1.12 t (CH_3), 2.31 s ($COCH_3$), 2.36-2.51 and 2.72-3.01 m (CH, CH, CH-cyclopropyl), 3.99 q (CO_2CH_2), 6.01-6.22 m (CH, CH-3,4-furyl), 7.18-7.24 m (CH, 2-furyl); PMR spectrum (XIIb), (δ, ppm): 1.23 t (CH_3), 2.17 s ($COCH_3$), 4.01 q (CO_2CH_2), 5.96-6.26 m and 7.15-7.20 m (3H, furyl). M/e 222 (M^+).

Methyl 2-(α-furyl)-3-acetylcyclopropanecarboxylate (XIIIa, b) was prepared from salt (V) and enone (VII), bp 115°C (1 mm), n_D^{25} 1.5092. IR spectrum (ν, cm^{-1}): 1710, 1740 (C=O). PMR spectrum (δ, ppm): 2.33 s (3H, $COCH_3$), 2.35-2.90 m (CH, CH-cyclopropyl), 3.54 s (CO_2CH_3), 5.97-6.23 m (CH, CH-3,4-furyl), 7.08-7.20 m (CH-2-furyl).

Ethyl 2-phenyl-3-acetylcyclopropanecarboxylate (XIVa, b) was prepared from the salt (II) and the enone (VIII), bp 134°C (1 mm), n_D^{25} 1.5225. IR spectrum (ν, cm^{-1}): 1715, 1735 (C=O). PMR spectrum (XIVa), (δ, ppm): 1.0 t (CH_3), 2.34 s ($COCH_3$), 2.40-2.62 m (CH, CH-cyclopropyl), 2.84-3.04 m (CH-cyclopropyl), 3.88 q (CO_2CH_2), 7.16 s (C_6H_5).

Methyl 2-phenyl-2-acetylcyclopropanecarboxylate (XVa,b) was prepared from salt (V) and enone (VIII), bp 115°C (1 mm), n_D^{25} 1.5393, IR spectrum (ν, cm^{-1}): 1710, 1740 (C=O). PMR spectrum (XVa), (δ, ppm): 2.29 s ($COCH_3$), 3.38 s (OCH_3), 2.36-3.10 m (CH, CH, CH-cyclopropyl), 7.13 s (C_6H_5). ^{1}H NMR spectrum (XVb) (δ, ppm): 2.18 s ($COCH_3$), 3.59 s (OCH_3), 2.36-3.10 m (CH, CH, CH-cyclopropyl), 7.13 s (C_6H_5).

Ethyl 2-(α-furyl)-3-benzoylcyclopropanecarboxylate (XVIa, b) was prepared from salt (II) and enone (IX). IR spectrum (ν, cm^{-1}): 1680, 1735 (C=O). PMR spectrum (δ, ppm): 1.13 t (3H, CH_3), 2.46-3.16 m and 3.50-3.75 m (CH, CH, CH-cyclopropyl), 3.98 q (CO_2CH_2), 6.0-6.25 m (CH, CH-3,4-furyl), 7.18-7.4 m (CH-2-furyl, CH, CH, CH-m, m, p-phenyl), 7.78-8.0 m (CH, CH-o,o-phenyl).

Ethyl 2-phenyl-3-benzoylcyclopropanecarboxylate (XVIIa,b) was prepared from salt (II) and enone (X), n_D^{25} 1.5850. IR spectrum (ν, cm^{-1}): 1680, 1730. PMR spectrum (δ, ppm): 1.03 t (CH_3), 2.56-3.48 m (CH, CH-cyclopropyl), 3.85 q (CO_2CH_2), 7.28-8.04 m (C_6H_5).

Ethyl 2-phenyl-3-cyclopropylcarbonylcyclopropanecarboxylate (XVIIIa,b) was prepared from salt (II) and enone (XI), bp 110-115°C ($2\cdot10^{-2}$ mm). IR spectrum (ν, cm^{-1}): 1695, 1730 (C=O). PMR spectrum (XVIIIa) (δ, ppm): 0.98 t (CH_3), 1.05-1.43 m (CH_2, CH_2-cyclopropyl), 2.47-2.78 m and 2.95-3.37 m (CH, CH, CH-cyclopropyl), 3.95 q (CO_2CH_2), 7.25 s (C_6H_5). PMR spectrum (XVIII b) (δ, ppm): 1.1 t (CH_3), 1.05-1.43 m (CH_2, CH_2-cyclopropyl), 2.47-2.78 m and 2.95-3.37 m (CH, CH, CH-cyclopropyl), 4.17 q (CO_2CH_2), 7.18 s (C_6H_5).

CONCLUSIONS

We worked out a modification of the method for the cyclopropanation of α,β-unsaturated ketones with ethyl(dimethylsulfuranylidene)acetate, generated in situ from a sulfonium salt with 85% KOH in the presence of a phase-transfer catalyst, and studied the stereochemistry of the polysubstituted cyclopropanes.

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