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Syntheses of Novel Acetylene Cyclopropanes

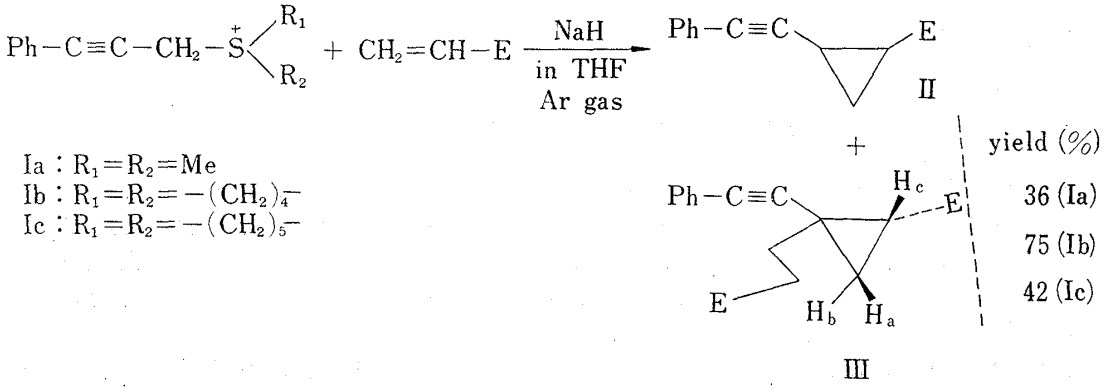
Julia and Martel have reported the synthesis of chrysanthemate by the reaction of 3, 3-dimethyl-2-propenyl phenyl sulfone with senecioate derivatives, independently.[1] While, we have investigated intensively the nucleophilic reactions of acetylene sulfonium[2] and sulfonyl[3] ylids. In this paper we extended the reactions of acetylene sulfonium ylids with electrophiles to α,β-unsaturated esters.

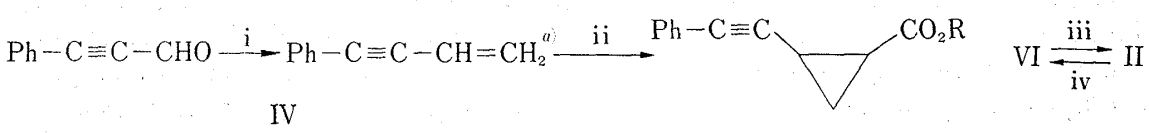
The mixture of 3-phenyl-2-propynyl sulfonium salts (I) and methyl acrylate was treated with sodium hydride. Anusual work-up and dry column chromatography[4] on silica gel gave two kinds of cyclopropane derivatives each of which was composed of two stereoisomers. The sturcture of the major component (*ca.* 90%) of the first was assigned to methyl *trans*-2-phenethynylcyclopropane carboxylate (IIa): $C_{13}H_{12}O_2$;[5] Mass Spectrum m/e=200(M^+); UV: 249 nm (log ε=4.31); IR: 2235, 1733 cm^{-1}; NMR[6] δ ppm: 1.35 (2H, m), 2.05 (2H, m), 3.70(3H, s). The configuration of IIa was deduced to be *trans* from the predominent formation of the *trans*-cyclopropanes in the reaction of carbonyl-stabilized sulfonium ylids with α,β-unsaturated esters.[7] The major component (*ca.* 60%) of the second was assigned to methyl 1-phenethynyl-1-(2-methoxycarbonyl)-ethylcyclopropane carboxylate (IIIa): $C_{17}H_{18}O_4$; Mass Spectrum m/e=286(M^+); UV; 249 nm(log ε=4.30); IR: 2230, 1740, 1734 cm^{-1}; NMR δ ppm: 1.0—2.9 (7H, m), 3.67 (3H, s), 3.75 (3H, s). The protons on the cyclopropane ring of IIIa were assignable using a shift reagent[6]: 2.40(1H, dd, Ha), 3.57(1H, dd, Hb), 4.15(1H, dd, Hc): J_{ab}=4.5Hz, J_{bc}=6.5, J_{ca}=8.3.

Acetylene sulfonium ylids are liable to produce allenic sulfides by 1,5-sigmatropic rearrangement.[8] In order to avoid this, 3-phenyl-2-propynyl sulfonium salts derived from tetramethylene sulfide or pentamethylene sulfide in place of dimethyl sulfide were chosen. In fact Ib and Ic afforded better results than Ia.

An independent synthesis of II was proceeded as shown in Chart 1 (IV→V→VI→II). Determination of the configuration of IIa was based on the degradation. The partial hydrogenation of IIa using 5% $Pd/CaCO_3$ (in MeOH–quinoline) gave VII (M^+=202, $\nu_{C=O}$= 1730 cm^{-1}, δ=6.42 ppm: 1H, d, J_1=11.5Hz, 5.07 ppm: J_1=11.5Hz, J_2=9.0), which was successively treated with OsO_4 and $NaIO_4$. The reaction mixture, which comprised benzaldehyde and methyl *trans*-2-formylcyclopropanecarboxylate, was converted directly to two esters according to Corey's method,[9] methyl benzoate and dimethyl *trans*-1,2-cyclopropanedicarboxylate. The scope and limitation are summarised in Table I.

1) M. Julia and A. G. Roualt, *Bull. Soc. Chim. France*, **1967**, 1411; J. Martel and C. Huynh, *ibid.*, **1967**, 985; J. Martel and G. Nomine, *Compt. Rend. (C)*, **1969**, 2199.
2) *a*) With benzaldehydes: A. Terada and Y. Kishida, *Chem. Pharm. Bull.* (Tokyo), **18**, 490, 497 (1970); *b*) With cyclic ketones: *idem*, *ibid.*, **18**, 991 (1970).
3) *a*) With benzaldehydes: M. Yoshimoto and Y. Kishida, *Chme. Pharm. Bull.* (Tokyo), **18**, 2518, 2528 (1970); *b*) With cyclic ketones: M. Yoshimoto, N. Ishida and Y. Kishida, *ibid.*, in press; *c*) With methyl acrylate: *idem*, *ibid.*, in preparation.
4) B. Loev and K. M. Snader, *Chem. Ind.* (London), **1965**, 15; B. Loev and M. M. Goodman, *ibid.*, **1967**, 2026.
5) All new compounds gave satisfactory combustion analyses.
6) Structure elucidation of cyclopropanes using a shift reagent is reported in the following joint paper: M. Yoshimoto, T. Hiraoka, H. Kuwano and Y. Kishida, *Chem. Pharm. Bull.* (Tokyo), **19**, 849 (1970)
7) J. Casanova and D. A. Rutolo, *Chem. Commun.*, **1967**, 1224; G. B. Payne and M. R. Johnson, *J. Org. Chem.*, **33**, 1285 (1968); H. Nozaki, M. Takaku and K. Kondo, *Tetrahedron*, **22**, 2145 (1966).
8) J. E. Baldwin, R. E. Hackler and D. P. Kelly, *Chem. Commun.*, **1968**, 1083; A. Terada and Y. Kishida, *Chem. Pharm. Bull.* (Tokyo), **17**, 966 (1969).
9) E. J. Corey, A. Katzenellenbogen, N. W. Gilman, S. A. Roman and B. W. Erickson, *J. Am. Chem. Soc.*, **90**, 5618 (1968).





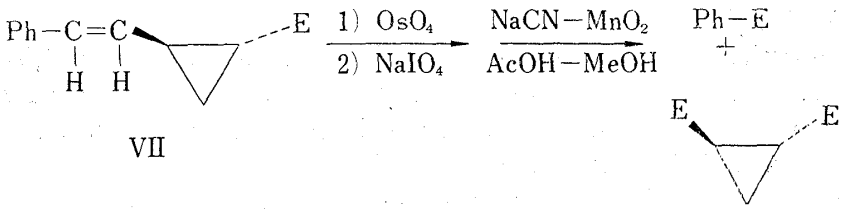
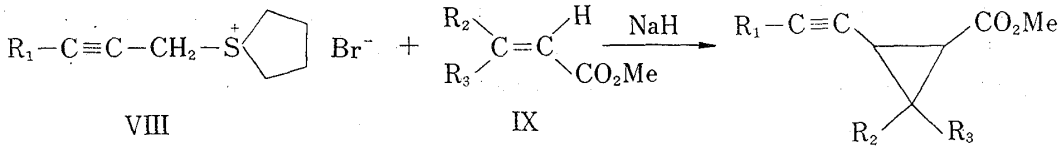


Chart 1

a) A.A. Petrovand and V.B. Lebedev, *Zhur. obsck. Khim*, 33, 3532 (1963).

TABLE I



Rnu	IX	R_1	R_2	R_3	Yield (%)	bp(mm Hg) (mp)	mp of $-CO_2H$
1	MA	Ph	H	H	75	108—110 (0.3)	89— 90 (*trans*) 84— 85 (*cis*)
2	MC	Ph	Me	H	11	110—115 (0.2)	
3	MS	Ph	Me	Me	trace		
4	MF	Ph	CO_2Me	H	19	150—155 (0.01)	205—207 (*trans*)
5	MM	Ph	H	CO_2Me	25	150—155 (0.01)	205—207 (*trans*)
6	MA	*p*-tolyl	H	H	43	112—113 (10^{-3})	95— 96
7	MA	*p*-Br-Ph	H	H	56	(57—59) (*trans*)	122—124 (*trans*)
8	MCi	*p*-Br-Ph	Ph	H	4		
9	MA	Me	H	H	57	108—110 (50)	87— 88
10	MC	Me	Me	H	33	106—108 (30)	54— 56
11	MA	H	H	H	6		

MA: methyl acrylate, MF: methyl fumarate, MC: methyl crotonate, MM: methyl maleate, MS:methyl senecioate, MCi: methyl cinnamate

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Reaction of N-(1-Cyanoalkyl)alkylideneamine N-Oxide with Carboxamides

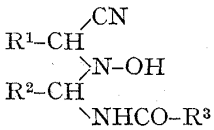
It is known that nitrones react as a 1,3-dipole with many unsaturated compounds to give cycloadducts, and with Grignard reagents and hydrogen cyanide to give hydroxylamines.[1)]

However, all these reactions, except the cycloadditions of isocyanate, isothiocyanate,[1)] and N-sulfinylaniline,[2)] involve a carbon nucleophile which attacks on the carbon atom of a nitrone group.

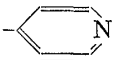
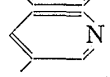
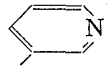
In this communication, we wish to report the first example of a non-cyclic 1,3-addition reaction of a nitrogen nucleophile with a nitrone.

When N-(1-cyanoalkyl)alkylideneamine N-oxide was dissolved in excess formamide at room temperature and the mixture was allowed to stand for 3—10 days, a crystalline product, consistent with the expected 1:1 adduct (I), was separated from the solution.

TABLE I. N-(1-Cyanoalkyl)N-(1′-carbonamidoalkyl) Hydroxylamine



I

(I)	R^1	R^2	R^3	mp (°C)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
a	Pr^n	Pr^i	H	148.5—149.0	$C_{10}H_{19}O_2N_3$	56.38	8.99	19.73	56.29	8.98	19.58
b	Pr^n	Pr^n	H	145.0—146.5	$C_{10}H_{19}O_2N_3$	56.38	8.99	19.73	56.56	8.83	19.77
c	Pr^i	Pr^n	H	134.0—135.0	$C_{10}H_{19}O_2N_3$	56.38	8.99	19.73	56.14	8.91	20.02
d	Pr^i	Pr^i	H	121.5—122.0	$C_{10}H_{19}O_2N_3$	56.38	8.99	19.73	56.51	8.91	19.46
e	Pr^n	Et	H	151.5—152.0	$C_9H_{17}O_2N_3$	54.32	8.61	21.12	54.10	8.55	21.71
f	Pr^i	Et	H	138.0—139.0	$C_9H_{17}O_2N_3$	54.32	8.61	21.12	54.21	8.52	20.71
g	Et	Pr^n	H	140.0—140.5	$C_9H_{17}O_2N_3$	54.32	8.61	21.12	54.48	8.59	21.05
h	Et	Pr^i	H	154.0—154.5	$C_9H_{17}O_2N_3$	54.32	8.61	21.12	54.21	8.65	21.16
i	Pr^i	Me	H	137.0—137.5	$C_8H_{15}O_2N_3$	51.87	8.16	22.69	52.16	8.44	22.69
j	Pr^i	Pr^i		155.5—156.0	$C_{15}H_{22}O_2N_4$	62.12	7.65	19.32	61.91	7.55	19.13
k	Pr^i	Pr^i		146.0—148.0	$C_{15}H_{22}O_2N_4$	62.12	7.65	19.32	62.24	7.47	19.37
l	Pr^n	Pr^i		150.0—150.5	$C_{15}H_{22}O_2N_4$	62.12	7.65	19.32	61.81	7.62	18.98

1) J. Harmer and A. Macaluso, *Chem. Rev.*, **64**, 473 (1964).
2) O. Tsuge, M. Tashiro, and S. Mataka, *Tetrahedron Letters*, **1968**, 3877.