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THE REACTION OF TROPONOID WITH YLIDE VI[1)]

A NOVEL SYNTHESIS OF UNSYMMETRIC BIPHENYL

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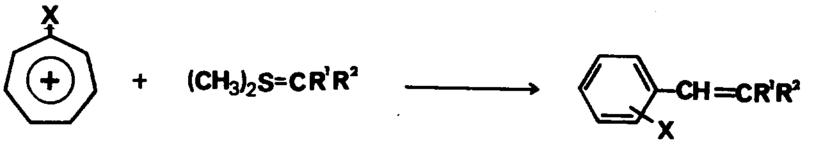
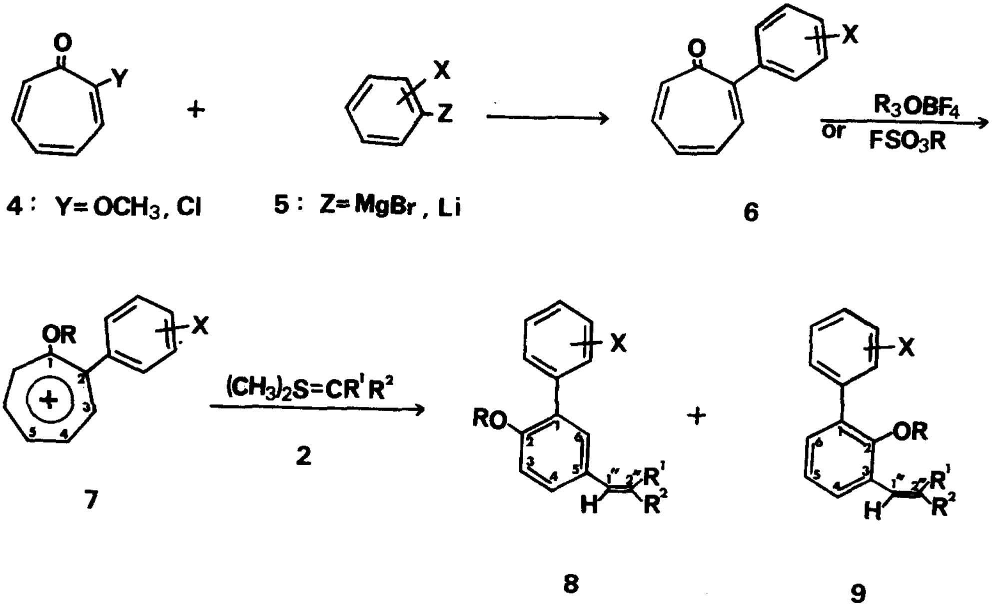
In an earlier paper[1)] we reported the reaction of tropylium- and alkoxytropylium ion (1) with some sulfur ylides (2) to afford styrene derivatives (3). As an extension of this reaction, it is expected to obtain some unsymmetric biphenyls, if phenyl group is introduced into the tropylium ions in the reactions.



1: X= H, OR   2   3: X=H, o-OR, p-OR

2-Phenylalkoxytropylium ion (7) was easily obtained by the treatment of 2-phenyltropone (6), which was prepared from methoxytropone (4, $Y=OCH_3$) and phenylmagnesium bromide[2)] or 2-chlorotropone (4, Y=Cl) and phenyllithium,[3)] with Meerwein reagent or magic methyl in methylene chloride. To a solution of 2-phenyltropone (6) in dry methylene chloride was added an equimolar amount of trimethyloxonium or triethyloxonium fluoroborate or methyl fluorosulfonate. The mixture was stirred for two to fifteen hours. Then the crystals precipitated (7) were collected by filtration or when no crystals precipitated, 7 could be obtained by crystallization by adding dry ether to the methylene chloride solution. The methylene chloride solution can be used to the next reaction without isolation of 7. The ion of 7 or the phenyltropylium ion solution was stirred with sulfonium ylide (2) in methylene chloride for several hours to



overnight at room temperature. The reaction mixture was washed with water. After general work up, silica gel dry column chromatography effected the isolation of unsymmetric biphenyls (8 and 9) and the starting phenyltropone (6). The results are shown in TABLE I. The structures of the unsymmetric biphenyls thus obtained were determined by the spectroscopic data (IR, UV, NMR and MS) and elemental analyses. For example, 8a (R=CH_3, R^1=R^2=CN): $C_{17}H_{12}ON_2$ (MS and elemental analysis); IR $\nu_{C\equiv N}$ 2220 cm^{-1}; UV λ_{max} (ethanol) 359.5 (log ε=4.43), 272.5(4.18), 246.0(4.17) nm; NMR (δ ppm, in $CDCl_3$) 3.92(3H, s: OCH_3) 7.11(1H, d, J=8.8 Hz: H-3), 7.3-7.65 (5H: H-phenyl), 7.69(1H, s: H-1") 7.86(1H, d, J=2.2: H-6), 7.97(1H, d of d, J=8.8 and 2.2: H-4). In the case using very stable sulfonium ylide (2a: R^1=R^2=CN, 2c: R^1=R^2=$COOC_2H_5$), 5-substituted-2-alkoxybiphenyls (8) were main products with traces of 3-substituted-2-alkoxybiphenyls (9). However, relatively reactive ylides (2b: R^1=H, R^2=$COOC_2H_5$, 2d: R^1=H, R^2=COC_6H_4-$NO_2{}^P$) afforded 9 as main products with 8 being byproducts. The reason of this difference of these product ratios due to ylides used would be explained by the

TABLE I

X	R	R^1	R^2	Yield %	Product ratio 8 : 9	Melting point
H	CH_3	CN	CN	52	only 8a	8a(129.5°)
H	C_2H_5	H	$COOC_2H_5$	84	1 : 2.3	8b(oil), 9b(oil)
H	C_2H_5	$COOC_2H_5$	$COOC_2H_5$	98	7 : 1*	8c(73.5°), 9c**
H	C_2H_5	CN	CN	86.8	only 8d	8d(113°)
H	C_2H_5	H	$COC_6H_4\text{-}NO_2{}^{p}$	86.5	1 : 3.1	8e(152°), 9e(131°)
$p\text{-}OCH_3$	C_2H_5	CN	CN	15.9	only 8f	8f(120°)
$p\text{-}OCH_3$	C_2H_5	H	$COC_6H_4\text{-}NO_2{}^{p}$	70.8	1 : 1.3	8g(138°), 9g(129°)
$m\text{-}OCH_3$	CH_3	CN	CN	58.1	only 8h	8h(160°)
$m\text{-}OCH_3$	CH_3	H	$COC_6H_4\text{-}NO_2{}^{p}$	95.4	1 : 1.7	8i(185°), 9i(148°)
$o\text{-}OCH_3$	CH_3	CN	CN	42.5	only 8j	8j(133.5°)
$o\text{-}OCH_3$	CH_3	H	$COC_6H_4\text{-}NO_2{}^{p}$	69.4	1 : 1.5	8k(197.5°), 9k(170°)
$p\text{-}CH_3$	CH_3	CN	CN	47.3	only 8l	8l(150.5°)
$p\text{-}CH_3$	CH_3	$COOC_2H_5$	$COOC_2H_5$	85.3	9 : 1*	8m(60°), 9m**
m-CHO $p\text{-}OCH_3$ 〉	CH_3	$COOC_2H_5$	$COOC_2H_5$	95	only 8n	8n(123°)
$n\text{-}COOCH_3$ $p\text{-}OCH_3$ 〉	CH_3	$COOC_2H_5$	$COOC_2H_5$	62	8 : 1*	8o(oil), 9o**

* based on the integration of NMR. ** not isolated.

TABLE II

Chemical shifts of ortho-alkoxy protons (OR) of 8 and 9 (in $CDCl_3$, δ ppm)

	$-OCH_2CH_3$			
	CH_2		CH_3	
	8	9	8	9
b	4.10	3.57	1.34	1.11
c	4.12	3.59	1.30	1.10
d	4.20	--	1.40	--
e	4.13	3.60	1.37	1.10
f	4.23	--	1.42	--
g	4.11	3.60	1.38	1.12

	$-OCH_3$	
	8	9
a	3.92	--
h	3.83(3.92)*	--
i	3.83(3.87)*	3.47
j	3.77(3.88)*	--
k	3.77(3.83)*	3.45
l	3.88	--
m	3.80	3.43
n	3.88(3.98)*	--
o	3.87	3.43

* These ortho OCH_3 protons could not be distinguished from those of substituent X.

steric interference at the reaction sites of both ylides and phenyltropylium ions (7). That is, the more hindered carbanions of 2a and 2c would attack the less hindered 4 and/or 5 position of 7 to afford 8[1].

For the structural determinations of these biphenyls, NMR was very effective. The coupling constants of olefinic protons of 8b and 9b were both 16 Hz suggesting the trans-configurations for them. The chemical shifts of 2-alkoxyprotons are shown in TABLE II. Methyl protons of 2-methoxy or methylene protons of 2-ethoxy of 9 exhibited signals at higher fields than those of 8. These diamagnetic shifts would be due to the anisotropy of 1-phenyl substituent whose plane situated vertically to that of the benzene ring, because of the release of the steric interference among the neighboring 1-, 2- and 3-substituents, and also due to the effect of the anisotropy of 1"-2" double bonds that are twisted to the plain of the benzene ring. The observation of these diamagnetic shifts was effective to the structure determination of biphenyls.

Unsymmetric biphenyls have been prepared by the Ullman synthesis[4], the decomposition of benzenediazonium salts in phenol[5] and by some other methods. However, these reactions require well-selected experimental reaction conditions and still give by-products. Recently, Omura reported the photochemical synthesis of unsymmetric biphenols[6]. This method gave biphenols in relatively good yield, but can be applied to limited targets.

We are now under investigation on the application of this new method to the synthesis of certain natural compound having the biphenyl moiety.

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