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1,3-BIS(PHENYLSULFONYL)BUTADIENES: SYNTHESIS APPLYING KNOEVENAGEL-TYPE CONDENSATION AND MICHAEL-TYPE ADDITION-CYCLIZATION WITH ENAMINES

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Summary: Knoevenagel-type condensation of 1,3-bis(phenylsulfonyl)propene with aldehydes provided electron-deficient dienes, 1,3-bis(phenylsulfonyl)butadiene derivatives, and one of these dienes, 4-[3,4-(methylenedioxy)]phenyl derivative was applied to Michael-type addition with enamines to form six-membered ring systems.

Electron-deficient dienes offer a useful method for the formation of five- and six-membered ring systems by addition-cyclization with nucleophiles such as sulfonium ylides and enamines, respectively.[1] Sulfonyl group (RSO_2-) should be efficient as a substituent of electron-deficient diene because of being an electron-withdrawing group and a transferable group after the addition-cyclization.[2] We wish to report 1) versatile synthesis of electron-deficient dienes, 1,3-bis-(phenylsulfonyl)butadienes (2) by applying Knoevenagel-type condensation of 1,3-bis(phenylsulfonyl)propene (1)[3], vinylogous to bis(phenylsulfonyl)methane[4], with aldehydes and 2) regioselective Michael-type addition-cyclization to 2c with enamines.[5]

In a typical procedure of the Knoevenagel-type condensation of 1, a solution of 1 (0.32g, 1mmol), piperonal (0.16g, 1mmol), and catalytic amounts of piperidine and acetic acid in benzene (20ml) was refluxed for 2 h with Dean-Stark apparatus. Usual work-up and recrystallization provided 0.40g (88%) of 2c. The results of the condensation with several aldehydes are summarized in Table 1.

The condensation is affected by steric hindrance, since the reaction of 1 with ketones such as cyclohexanone, 2-octanone, and acetophenone did not occur at all and 1-methyl- and 2-methyl-1,3-bis(phenylsulfonyl)propene condensed with benzaldehyde in refluxing toluene for 20 h to give 1-methyl derivative (35%) and 2-methyl derivative (5%), respectively.

Scheme

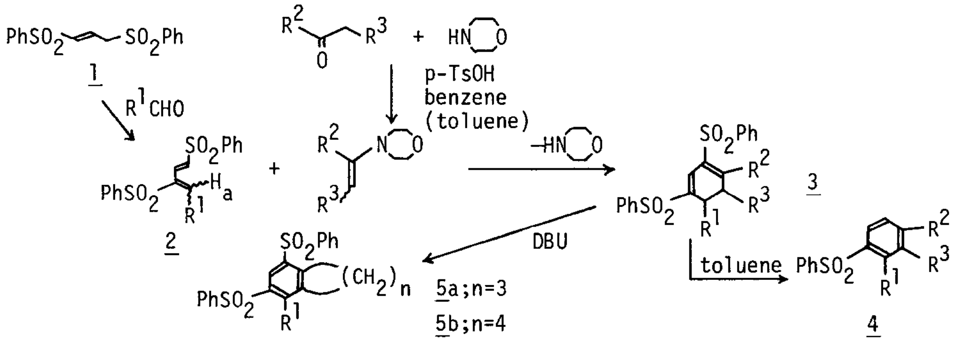
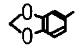
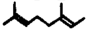


Table 1. Knoevenagel-type condensation of 1 with aldehydes[6]

entry	aldehyde	time(h)	product; R^1		yield(%)
1	benzaldehyde	3	Ph-	2a	83^a
2	*trans*-cinnamaldehyde	5	PhCH=CH-	2b	87^b
3	piperonal	2		2c	88^a
4	isobutyraldehyde	24	$(CH_3)_2CH$-	2d	$72^{a,c}(90)^{a,d}$
5	geranial	6		2e	55^b

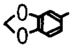
a) Integral value of H_a by NMR(FX-200) suggested that 2 was a single stereoisomer [R^1, H_a(ppm): Ph, 8.14(s);  , 8.07(s); $(CH_3)_2CH$, 7.19(d)]. b) Stereochemistry was not confirmed. c) benzene, 50 °C, d) pentane, reflux.

Table 2. Michael-type addition-cyclization to 2c[6]

entry	ketone	time(h)	product R^2	R^3		yield(%)
1	cyclopentanone	5	$-(CH_2)_3-$		3a	$74^a(87)$
2	cyclohexanone	7	$-(CH_2)_4-$		3b	$87^a(94)$
3	cycloheptanone	9	$-(CH_2)_5-$		3c	$81^a(86)$
4	4-t-butylcyclohexanone	9	$-(CH_2)_2CH(t\text{-}Bu)CH_2-$		3d	47^a
5	4-t-butylcyclohexanone	18	$-(CH_2)_2CH(t\text{-}Bu)CH_2-$		4a	28^b
6	diethyl ketone	30	CH_3CH_2-	CH_3-	4b	55^b

a) benzene, reflux, b) toluene, reflux. Figures in parentheses are yields of the reaction of 2c with the corresponding enamines in refluxing THF.

Using 2c, Michael-type addition-cyclization was investigated. The results are shown in Table 2. Although 2c reacted with enamines to give 3 in high yields (entry 1, 2, and 3), the reaction was carried out using ketones and morpholine because of the instability of enamines toward oxygen. In the typical procedure, a solution of 2c (0.45g, 1mmol), cyclohexanone (0.12g, 1.2mmol), morpholine (0.10g, 1.2mmol), and a catalytic amount of p-TsOH in benzene (20ml) was refluxed for 7 h with Dean-Stark apparatus. Usual work-up and preparative TLC provided 0.46g (87%) of 3b. In all cases, the reaction occurred regioselectively to form six-membered ring systems. The reaction in refluxing toluene induced aromatization to 4 by the elimination of one phenylsulfinic acid (entry 5 and 6). Acyclic ketones such as acetophenone and 2-octanone and aldehydes did not react with 2c.

Treatment of 3a and 3b (0.5mmol) with DBU (0.55mmol) in refluxing toluene (2ml) quantitatively provided unusual aromatic compounds 5a and 5b, respectively. Thus, these preliminary studies suggest this addition-cyclization is a good approach for the formation of benzene ring systems.

References and notes: 1) F.E.Ziegler and E.B.Spitzner, J.Am.Chem.Soc., 95, 7146 (1973); T.Minami, T.Yamanouchi, S.Takenaka, and I.Hirao, Tetrahedron Lett., 24, 767 (1983) and references cited therein. 2) P.D.Magnus, Tetrahedron, 33, 2019 (1977). 3) a colorless crystalline solid, mp 101-102 °C, only E-isomer by NMR. 4) H.Stetter and K.Steinbeck, Justus Liebigs Ann.Chem., 1974, 1315. 5) J.d'Angelo, Tetrahedron, 32, 2979 (1976). 6) All product obtained here exhibited satisfactory spectral and physical properties.

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