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Synthesis of Some Novel 2,3-diaryl-Butadiene Analogues

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Abstract: In present paper, the 2,3-diaryl-butadiene analogues were synthesized as anti-cancer agents. The structures were confirmed by ^{1}HNMR and elemental analysis.

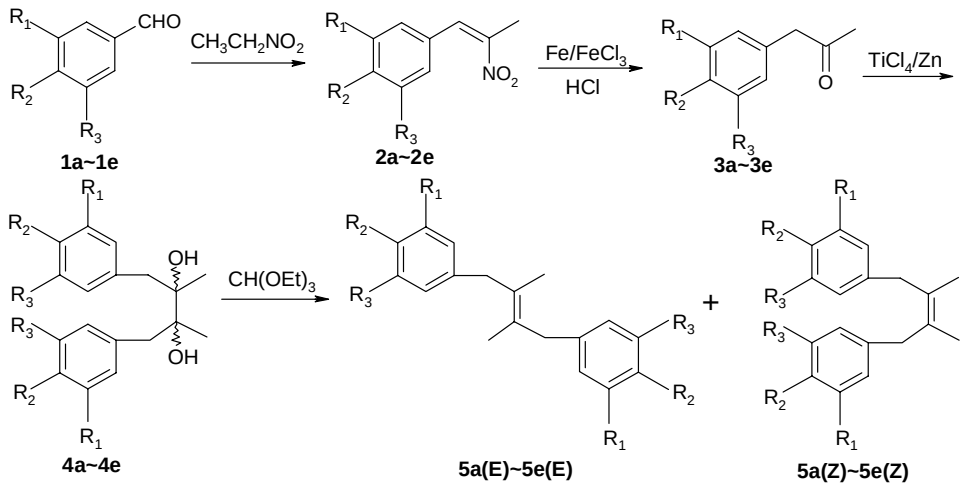
Keywords: 2,3-Dibenzyl-2-butene, coupling reaction, carbonyl compounds.

The reductive coupling of carbonyl compounds is an important method of carbon-carbon bond formation. The reaction can be used in both an inter-and intramolecular manner. It is important for the formation of olefins. Mukaiyama T., *et al*[1] reported that the reductive coupling of ketones with $TiCl_4$/Zn in tetrahydrofuran (THF) afforded the corresponding pinacols or olefins in high yields. The pinacols were obtained at 0℃. After heating, the deoxygenation reaction of pinacols afforded olefins[2]. In the present paper, we report the reductive couplings of phenylacetones (**3a-3e**) with $TiCl_4$/Zn to afford the corresponding pinacoles when the coupling reaction was carried out at 0℃ or at reflux temperature. The control factors of stereochemistry of the products are not clear. However, we have found that olefins were obtained by treatment of the pinacols with ethyl orthoformate.

2,3-Diaryl-butadiene was isolated from the stem of *Anogeissus acuminata(Roxb. ex DC) Guill. and* Perr. *var. Lanceolate* wall *ex* CB Clarke. This kind of compounds showed cytotoxicity for various cancer cell lines and some of them also showed inhibitory activity against HIV-1 reverse transcriptase[3-6] in vitro. For search new anti-cancer agents, we synthesized the analogs of 2,3-diaryl-butadiene for bioscreening. The compound **3a~3e** were used as starting materials (**Scheme 1**).

3a~3e were synthesized by reduction and hydrolysis with Fe-$FeCl_3$/conc. HCl of the nitrostyrenes **2a~2e**, which were prepared from the corresponding benzaldehydes in high yields. The threo erythro mixtures of 2,3-diaryl-2-butanediols **4a~4e** were obtained by reductive couplings of the **3a~3e** with $TiCl_4$-Zn in tetrahydrofuran (THF). Treatment of the compounds **4a~4e** with ethyl orthoformate in the presence of benzoic acid afforded the corresponding (*E*) and (*Z*)-butenes[7] in a ratio of 1∶1, yield>90%. The *E* and *Z* isomers could be separated easily by simple recrystallization from ethyl alcohol. We deduced the mechanism of this reaction as shown in **Scheme 2**. Thus, deoxygenations of *cis*- and *trans*-butanediols occured at approximately the same rate.

Scheme 1



1a~1e **2a~2e** **3a~3e** **4a~4e** **5a(E)~5e(E)** **5a(Z)~5e(Z)**

a: $R_1=R_2=R_3=OCH_3$
b: $R_1+R_2=OCH_2O$, $R_3=OCH_3$
c: $R_1=R_2=OCH_3$, $R_3=H$
d: $R_1+R_2=OCH_2O$, $R_3=H$
e: $R_1=R_3=OCH_3$, $R_2=H$

The physical properties and ^{1}HNMR data of compounds **5a**~**5e** are shown in **Table 1** and **Table 2**.

Table 1 The Physical Properties of compounds **5a**~**5e**

Compound	Color and state	mp℃
5a(E)	Colorless crystals	121-122
5a(Z)	Yellowish oil	
5b(E)	Colorless crystals	115-116
5b(Z)	Yellowish oil	
5c(E)	Colorless crystals	76-78
5c(Z)	Yellowish oil	
5d(E)	Colorless crystals	118-119
5d(Z)	Yellowish oil	
5e(E)	Colorless crystals	68-69
5e(Z)	Yellowish oil	

Scheme 2

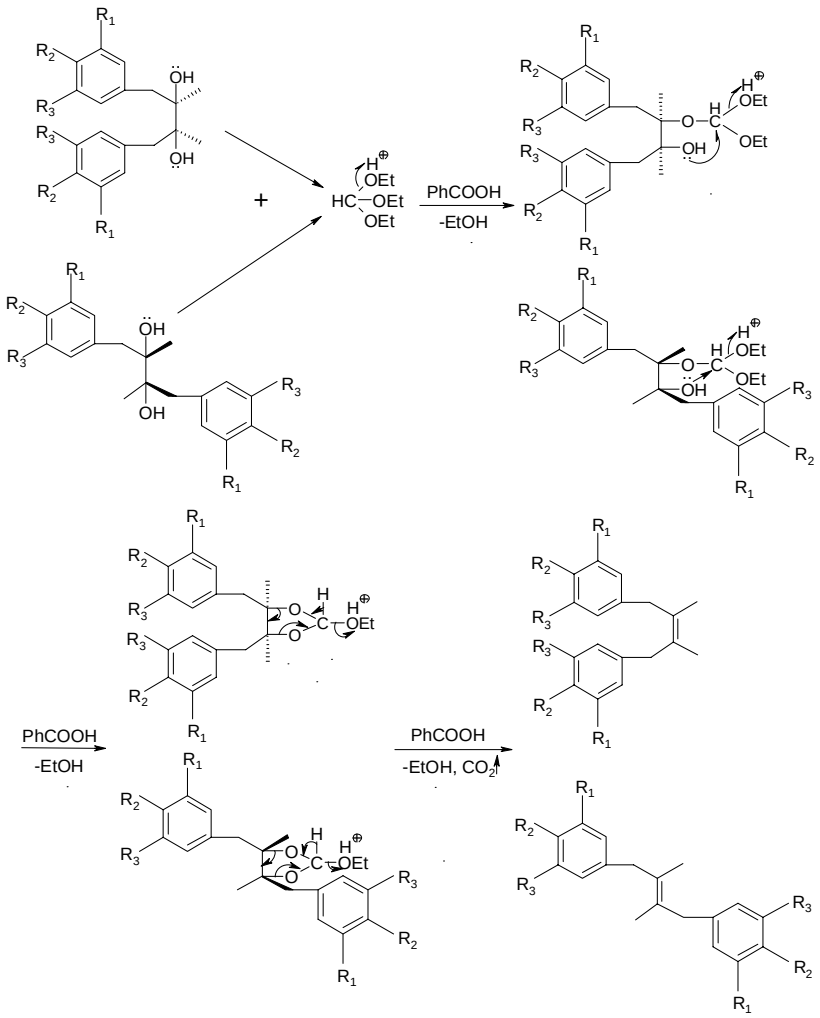


Table 2 The ^{1}HNMR (90MHz, $CDCl_3$) data and elemental analysis of compounds **5a~5e**

	^{1}HNMR(δ)					Anal. Calcd.		Found	
	ArH	OCH_2O	CH_3O	CH_2	CH_3	C	H	C	H
5a(E)	6.49s		3.86s	3.41m	1.63s	69.20	7.74	69.15	7.50
5a(Z)	6.60s		3.88s	3.49m	1.70s	69.20	7.74	69.08	7.65
5b(E)	6.33d	5.92s	3.87s	3.41m	1.68s	68.73	6.29	68.70	6.33
5b(Z)	6.34m	5.92s	3.88s	3.40d	1.72s	68.73	6.29	68.98	6.30
5c(E)	6.76m		3.85s, 3.83s	3.45d	1.75s	74.13	7.92	74.13	7.88
5c(Z)	6.68m		3.86s, 3.84s	3.48d	1.68s	74.13	7.92	74.09	7.90
5d(E)	6.65m	5.91s		3.37s	1.72s	74.07	6.17	74.03	6.15
5d(Z)	6.64m	5.92s		3.44s	1.69s	74.07	6.17	74.05	6.13
5e(E)	7.02s, 6.92s, 6.44m		3.82s, 3.78s	3.38s	1.68s	74.13	7.92	74.08	7.90
5e(Z)	7.03s, 6.92s, 6.44m		3.80s	3.39d	1.69s	74.13	7.92	74.10	7.89

The biological evaluations of these compounds were summarized in **Table 3**.

Table 3 The anti-cancer biological evalutions of compounds **5b(*E*), 5b(*Z*), 5c(*E*), 5c(*Z*), 5e(*E*)** and **5e(*Z*)**

Compound	Cell model	IC_{50}(μ g/ml)	Results
5b(*E*) **5b(*Z*)**	KB	<1	7++
	HCT-8	<1	++
	Bel 7402	<1	++
	A 2780	<1	++
	L 1210	<1	++
5c(*E*)	KB	<1	++
	HCT-8	<1	++
	Bel 7402	<10	+
	A 2780	<1	++
	L 1210	<1	++
5c(*Z*)	KB	<10	+
	HCT-8	<1	++
	Bel 7402	<1	++
	A 2780	<1	++
	L 1210	<1	++
5e(*E*) **5e(*Z*)**	KB	<1	++
	HCT-8	<1	++
	Bel 7402	<1	++
	A 2780	<1	++
	L 1210	<1	++

IC_{50}=concentration required to inhibit 50%"+"=weak activity; "++"=stronger activity of host cells.

References and Notes

1. T. Mukaiyama, T. Sato, J. Hanna, *Chem. Lett.*, **1973**, 1041.
2. J.E. McMurry, *Chem. Rev.*, **1989**, *89*, 1513.
3. M. Rimando, J. M. Pezzuto, N, R. Farnsworth *et al*., 206th ACS National Meeting, Division of Medicinal Chemistry, Chicago, IL, August 22-27, **1993**, MEDI.211
4. Y. Lee, Y. B. Han, W. S. Woo, *et al.*, *Saengyak Hakhoechi*(Eng), **1990**, *21*(4), 270.
5. J. L. Belletire, D. F. Fry, S. L. Fremont, *J. Nat. Prod.*, **1992**, *55*(2), 184.
6. C. C. Chen, W. C. Hsin, Y. L. Huang, *J. Nat. Prod.*, **1998**, *61*(2), 227.
7. All key intermediates and final products in **Scheme 1** gave the correct elemental analysis (± 0.4%)

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