A New Synthesis of 1,4-Diaryl-1,3-butadienes Utilizing the Anil Synthesis

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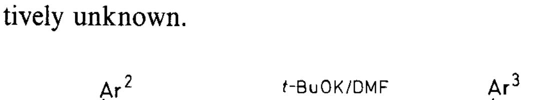
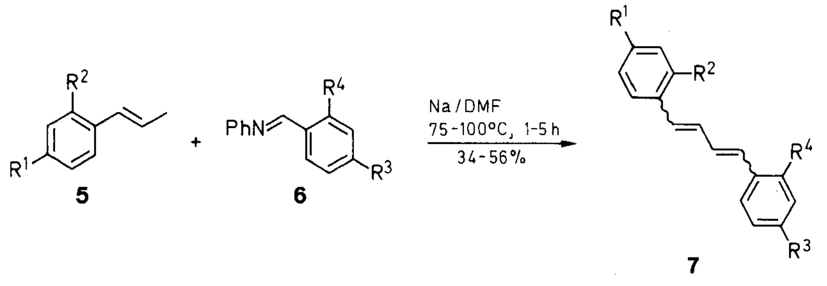
The anil synthesis was employed in the preparation of 1,4-diarylsubstituted 1,3-butadienes **7** from 1-arylpropenes **5** and *N*-arylideneanilines (aromatic Schiff bases) **6** in dimethylformamide solution and a strong base as catalyst obtained *in situ* by reacting metallic sodium with this solvent.

The Wittig reaction is a well-established method for the preparation of carbon–carbon double bonds.[1] However, the usual requirements of expensive phosphines and organic halides, one equivalent of strong base, the two-step preparation of the ylide, and lack of environmentally safe disposal of the phosphone product all combine to make the Wittig reaction not amenable to large scale preparations. The Siegrist reaction, that is reaction of aromatic Schiff bases **1** with methyl substituted aromatic compounds **2** in the presence of potassium *tert*-butoxide or powdered potassium hydroxide in dimethylformamide to yield stilbenes **3**, is an attractive alternative. Although Siegrist in a series of publications and patents[2-4] has utilized the anil synthesis for the preparation of over one thousand substituted stilbenes, this reaction is still relatively unknown.



This research group was attracted to the anil synthesis because of the facile preparation or availability of reactants, the recyclability of the aromatic amines **4** produced and the fewer experimental steps involved. The objective was to extend the anil synthesis to the synthesis of a number of dienes and tetraenes as starting materials for the preparation of aromatic anhydrides, via a Diels–Alder reaction with maleic anhydride. The dianhydrides could then be used to synthesize polyimides by the reaction with diamines. Herein we report the preparation of several dienes and tetraenes by a modification of the Siegrist reaction.[5]

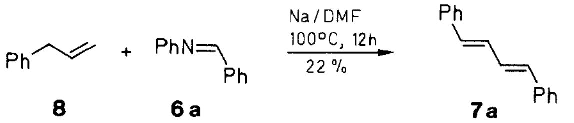
When sodium is reacted with dimethylformamide, three anionic species result with a preponderance of sodium dimethylamide above 100 °C.[6] The sodium dimethylaminoformamidide and sodium *N,N*-dimethyl-2-(dimethylamino)-2-oxidoethanamide[6] can essentially by regenerated by sodium dimethylamide when in the presence of more dimethylformamide, by analogy with the behavior of sodium hydride[7] and other alkali amide derivatives.[8,9] This medium, abbreviated below as Na/DMF, has the advantage of being effective in preparing *trans*-stilbene (40% yield)[10] from excess toluene and **6a**, whereas potassium *tert*-butoxide with the more reactive 4-chlorotoluene gave a 37% yield of the corresponding stilbene.[4,11] The reaction of 1-arylpropenes **5** and aromatic Schiff bases **6** gives the corresponding dienes (or tetraenes) **7**. The solubility of sodium dimethylamide in *N,N*-dimethylformamide is limited; however, the presence of sodium *N,N*-dimethyl-2-(dimethylamino)-2-oxidoethanamide may act as a "complex base"[12] increasing the basicity by dissolving more of sodium dimethylamide. The effects of other additives such as 2-methyl-2-propanol on these reactions are currently being investigated.



5	R1	R2	6	R3	R4
a (*trans*)	H	H	**a**	H	H
b	H	2-($CH_3CH=CH$)$C_6H_4OCH_2O$	**b**	4-($PhN=CH$)$C_6H_4OCH_2O$	H
c (*trans*)	MeO	H	**c**	H	2-($PhN=CH$)$C_6H_4OCH_2O$
			d	MeO	H

7	R1	R2	R3	R4
a	H	H	H	H
b	MeO	H	H	H
c	MeO	H	4-(4-$MeOC_6H_4((CH=CH)_2)C_6H_4OCH_2O$	H
d	H	H	H	2-($Ph(CH=CH)_2)C_6H_4OCH_2O$
e	H	H	4-($Ph(CH=CH)_2)C_6H_4OCH_2O$	H
f	MeO	H	H	2-(4-$MeOC_6H_4(CH=CH)_2)C_6H_4OCH_2O$

The mechanism by which **7** is formed probably involves the initial generation of a carbanion by abstraction of a methyl hydrogen.[3] This carbanion then adds to the imine to generate an amine. A second hydrogen abstraction with elimination of aniline then gives the desired product **7**. In the anil reaction[13] additional conjugated double bonds, heterocyclic substituents, aza nitrogens, etc., increase the acidicity of the methyl hydrogens to the point where powdered potassium hydroxide is sufficiently basic for the reaction to proceed. Therefore the reaction of (*E*)-1-methoxy-4-(1-propenyl)benzene (**5c**) with **6a** in the presence of powdered potassium hydroxide was attempted but no diene formed.



Although allylbenzene **8** isomerizes in the presence of strong base,[14–16] the simultaneous reaction with **6a** produces a lower yield (see Table 1) of the expected diene **7a** with formation of uncharacterized byproducts arising from olefin isomerization. The major difference in these two reactions is the ease of ionization of (*E*)-*β*-methylstyrene compared to allylbenzene (pK = 32 ± 2).[16] This suggests that isomerization must be done first as a

Table 1. Preparation of Dienes **7** from Aromatic Schiff Bases **6** and Arylpropenes **5**

Starting Materials	Reaction Conditions			Product	Yield[b] (%)	mp (°C)[c] (solvent)	Molecular Formula[d] or Lit. mp (°C)
	Ratio **5**:**6**	Temp. (°C)	Time[a] (h)				
5a + **6a**	1:1	90	2	**7a**	54	150–153 (EtOH)	152–152.5[17]
5c + **6a**	1:1	90	4	**7b**	50	160–162 (EtOH)	163–164[18]
5c + **6b**	2:1	100	5	**7c**	54	246–248 (DMSO)	$C_{35}H_{32}O_4$ (516.6)
5b + **6a**	1:2	75	1[e,f]	**7d**	34	190–192[g] (benzene)	$C_{33}H_{28}O_2$ (456.6)
5a + **6c**	2:1	75	1[e,f,h]	**7d**	54		
5a + **6b**	2:1	100	3	**7e**	56	233–235 (THF)	$C_{33}H_{28}O_2$ (456.6)
5c + **6c**	2:1	100	3	**7f**	50	240–241 (DMSO)	$C_{35}H_{32}O_4$ (516.6)

[a] Similar reactions using *t*-BuOK were run for an average of 90 min at 90 °C.[13]

[b] No optimization was attempted. This yield is after one recrystallization, when the original crude dry material weighed between 70–90% of theory. A similar behavior has been reported.[4]

[c] The melting points are for the materials whose yields are reported here. They are uncorrected, measured on a Fisher-Johns melting point apparatus.

[d] Satisfactory microanalyses obtained: C ±0.23, H ±0.13, O ±0.18.

[e] Monitored by Milton Roy HPLC instrument using a CM4000 multiple delivery system, auto injector A1000, spectromonitor 3100 with variable wavelength, CI 10B integrator and LDC plotter by means of a 5 µm ODS2 reversed-phase column and methanol as eluent at 1000 mL/min flow rate.

[f] Reaction was later studied by reversed phase HPLC indicating a reaction time of 30 min at 75 °C.[e]

[g] Initially there is some liquification at ~185 °C, resolidifying while heating to melt from 193–195 °C. The same sample is cooled and reheated to the melting point stated.

[h] Double quantity of reactants was used as indicated in the experimental but sodium and volume of DMF were as per the general procedure in the experimental.

Table 2. Spectroscopic Data of the 1,3-Butadienes **7** Prepared

Product	FTIR ($CDCl_3$) ν (cm^{-1})	UV (THF) λ_{max} (nm) (ε)	^{1}H-NMR ($CDCl_3$/TMS) δ, J (Hz)	MS (EI, 70 eV) m/z (%)
7a	3083, 3063, 3028, 1612, 1595, 1492, 1446	319[a] (46900)[b], 330 (54800), 344 (35800)[b]	6.63–6.77 (tt, 2H, H-2), 6.92–7.06 (tt, 2H, H-1), 7.21–7.40 (m, 10H_{arom})	
7b	3082, 3062, 3029, 2960, 2936, 2912, 2839, 1603, 1596, 1575, 1512, 1508	340[c] (55200)	3.82 (s, 3H, OCH_3), 6.57–7.03 (m, 6H), 7.10–7.46 (m, 7H_{arom})	
7c	3014, 2956, 2973, 2911, 2837, 1600, 1505[d]	334 (105000)[b], 346 (123000), 364 (95300)[b]	–[d]	516[e] (M^+, 8.4), 121 (100)
7d	3082, 3064, 3027, 1595, 1577, 1485, 1457, 1448, 1410	338 (85700)	5.84 (s, 2H, OCH_2O), 6.58–6.62 (m, 2H), 6.87–7.14 (m, 8H), 7.21–7.60 (m, 16H_{arom})	456[f] (M^+, 12.2), 117 (100)
7e	3016, 2993, 1596, 1507, 1228, 1174, 1031, 1007[d]	323 (78600)[b], 338 (94700), 355 (73400)[b]	–[d]	456 (M^+, 89.3), 91 (100)
7f	3041, 3031, 3008, 2998, 2985, 2960, 2948, 2932, 2904, 2832, 1600, 1481, 1459, 1436[d]	348 (95000)	–[d]	516 (M^+, 29.6), 147 (100)

[a] In absolute EtOH λ_{max}(nm) (ε) = 328 (52500), 345 (33900).[17]

[b] Denotes a shoulder.

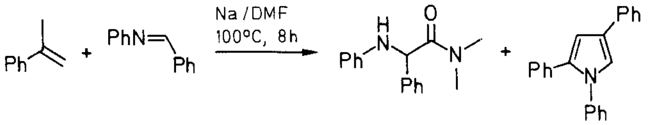
[c] In 95% EtOH λ_{max}(nm) (ε) = 361 (30500), 342.5 (44700), 331 (37500).[18]

[d] Poor solubility. FTIR (KBr), ^{1}H-NMR not obtained.

[e] HRMS calc. for $C_{35}H_{32}O_4$ (M^+): 516.230; found 516.241.

[f] HRMS calc. for $C_{33}H_{28}O_2$ (M^+): 456.209; found 456.207.

separate step to improve the yield. Combinations such as **5a** and **6c**, and **5b** and **6a** give the identical product **7d** varying only in quantity. This demonstrates the generality of the reaction. The less reactive propene compound **9** with one equivalent of **6a** gives low yields of **10** and 1,2,4-triphenylpyrrole (**11**). Compound **10** is probably an addition compound of **6a** and sodium dimethylaminoformamidide. On the other hand, **11** may arise from initial attack of the carbanion on the Schiff base with an intramolecular ring formation followed by oxidation. Thus the acidity of the hydrogens in the methyl group plays an important role in the anil synthesis between 1-, 2-, and 3-arylpropenes with aromatic imines.



9 **6a** **10** 12% **11** 3%

The FTIR spectra were obtained on an Analect AQS-18 FTIR Spectrophotometer and the UV spectra on a Unicam 850 spectrophotometer at 23°C. The ^1H-NMR spectra were recorded on a Varian XL-200 Spectrometer. Mass spectra were obtained on an HP5984A mass spectrometer.

Mixing the commercial (Aldrich) amine and aldehyde in benzene, removal of water by azeotropic distillation, and recrystallization from MeOH gave the pure Schiff bases **6a,d.** The imine **6** was prepared as reported.[19] DMF reagent grade was purchased from Anachemia and contains 0.15% H_2O. Sodium metal was a BDH product. Microanalyses for the compounds were done by Galbraith Laboratories, Knoxville, Tennessee, USA; except for **5b**, which was analyzed by Guelph Chemical Laboratories, Guelph, Ontario, Canada.

4,4'-Methylenedioxybis(phenylmethylene)dianiline (6b):

4,4'-Methylenedioxydibenzaldehyde: A mixture of 4-hydroxybenzaldehyde (12.2 g, 0.100 mol) and aq KOH 45.8% (12.2 g, 0.100 mol HO^-) is refluxed in benzene (50 mL) until no more water separates into the Dean-Stark trap (~ 1 h). The benzene is evaporated at reduced pressure. DMF (50 mL) and CH_2Br_2 (9.20 g, 0.053 mol) are added successively to the solid residue. The mixture is heated and stirred for 2 h at 80 °C. The product is precipitated by pouring the DMF mixture into H_2O (200 mL). A sample is purified to mp 84–85 °C (petroleum ether) and characterized.

FTIR ($CDCl_3$): ν = 2995 w, 2935 w, 2905 w, 2834, 2806, 2742, 1696, 1684, 1598, 1582, 1507, 1244, 1216, 1161, 1143, 1106, 1041, 1015, 1008 cm^{-1}.

^1H-NMR ($CDCl_3$/TMS): δ = 5.90 (s, 2H, OCH_2), 7.21–7.27 (m, 4H_{arom}), 7.85–7.91 (m, 4H_{arom}), 9.92 (s, 2H, CHO).

4,4'-Methylenedioxybis(phenylmethylene)dianiline (**6b**): To the dried reddish solid precipitate is added aniline (18.6 g, 2.00 mol) and benzene (50 mL), and the mixture is refluxed until no more H_2O separates into the Dean-Stark trap (~ 1 h). On cooling, **6b** crystallizes, is separated by suction-filtration and washed with a minimum quantity of benzene. The filtrate is reduced to one third of the volume and on cooling a second crop is obtained; yield: 38.2 g (94%); flakes mp 148–151 °C (benzene).

$C_{27}H_{22}N_2O_2$	calc.	C 79.78	H 5.46	N 6.89
(406.5)	found	79.97	5.43	6.65

FTIR ($CDCl_3$): ν = 3082, 3068, 3033, 2886, 1627, 1606, 1589, 1512, 1485, 1451, 1423, 1413, 1305, 1214, 1166, 1143, 1040, 1023 cm^{-1}.

^1H-NMR ($CDCl_3$/TMS): δ = 5.85 (s, 2H, OCH_2O), 7.17–7.25 (m, 10H, =NP), 7.33–7.41 (m, 4H_{arom}), 7.81–7.89 (m, 4H_{arom}), 8.38 (s, 2H, CHNPh).

Preparation of Na/DMF; General Procedure:

To DMF (40 mL) is added metallic Na (1.0 g, 0.043 mol) in seven portions at 105–110 °C under a slow stream of N_2 and with stirring. Additional portions of Na are introduced after the initial vigorous reaction abates. The addition of Na takes 15 min. The mixture is brought to the desired temperature (see Table 1) and the reactants are added using DMF (10 mL) as solvent.

2,2'-Methylenedioxybis(phenyl-1-propene):

To 2-propenylphenol[20] (17 g, 0.127 mol) is added successively KOH (8.40 g, 0.127 mol HO^-) and MeOH (50 mL) and the mixture is warmed to dissolve the solids. The MeOH is evaporated under reduced pressure. To the residue is added DMF (50 mL) and CH_2Br_2 (12.0 g, 0.069 mol) and heated at 80 °C for 1 h. After this period H_2O (200 mL) is added. The aqueous mixture is extracted with $CHCl_3$ (3 × 30 mL) and the organic phase is dried (Na_2SO_4). Removal of $CHCl_3$ under reduced pressure leaves a solid residue, which recrystallizes from MeOH as needles mp 74–75 °C; yield: 14.9 g (84%).

$C_{19}H_{20}O_2$	calc.	C 81.40	H 7.19.
(280.4)	found	81.61	7.45.

FTIR ($CDCl_3$): ν = 3074, 3038, 3012, 2067, 2935, 2915, 2882, 2854, 1599, 1578, 1486, 1452, 1410, 1381, 1321, 1292, 1231 (s), 1192, 1163, 1140, 1112, 1087, 1050, 1011 (s), 971 cm^{-1}.

^1H-NMR ($CDCl_3$/TMS): δ = 1.86 (dd, 6H, $J_{1,3}$ = 1.8 Hz, $J_{1,2}$ = 6.6 Hz, CH_3), 5.75 (s, 2H, OCH_2O), 6.10–6.30 (m, 2H, H 2), 6.68 (dq, 2H, $J_{2,3}$ = 16 Hz, H 1), 6.95–7.03 (m, 2H_{arom}, H 3'), 7.16–7.20 (m, 4H_{arom}), 7.40 (br d, 2H_{arom}, $J_{5',6'}$ = 8 Hz, H 6').

Preparation of 1,4-Diaryl-1,3-butadienes 7; General Procedure:

To the Na/DMF mixture (40 mL) prepared as above, is added a solution of Schiff base **6** (0.01 mol of imine groups) and arylpropene **5** (0.01 mol of methyl groups) in DMF (10 mL), at the reaction temperature stated in Table 1.

Disappearance of reactants is monitored by taking aliquots (10 μL), diluting with MeOH (10.0 mL), and injecting the sample into a high pressure liquid chromatograph (see footnotes e and f of Table 1). After the specified time (see Table 1) the mixture is poured into H_2O (150 mL). The precipitate is removed by filtration, washed with H_2O (50 mL), and MeOH (20 mL), dried, weighed, recrystallized, is weighed again to determine the reported yield in Table 1.

N,N-Dimethyl-α-(phenylamino)benzeneacetamide (10) and 1,2,4-Triphenylpyrrole (11):

Benzylideneaniline (**6a**; 1.81 g, 0.010 mol) and 2-phenylpropene (1.18 g, 0.010 mol) are heated at 100 °C for 8 h in Na/DMF (50 mL) until there is no more Schiff base. The mixture is poured into H_2O (150 mL) and extracted with Et_2O (3 × 70 mL). The organic phase is dried (Na_2SO_4) and the solvent is evaporated under reduced pressure to leave a reddish oil. EtOH (5 mL) is added and **10** crystallizes slowly; yield: 0.3 g (12%). Recrystallization from EtOH gives colorless prisms mp 160–162 °C (Lit.[21] mp 153–155 °C, HCl salt 198–200 °C):

$C_{16}H_{18}N_2O$	calc.	C 75.56	H 7.13	N 11.01
(254.3)	found	75.73	7.16	11.04

FTIR ($CDCl_3$): ν = 1653 (C=O), 3401 (NH) cm^{-1}.

^1H-NMR ($CDCl_3$/TMS): δ = 2.97 (s, 3H, NCH_3), 3.05 (s, 3H, NCH_3), 5.26 (d, 1H, J = 7.6 Hz, Hα), 5.42 (d, 1H, NH), 6.60–6.71 (m, 3H, H_{arom}), 7.07–7.17 (m, 2H_{arom}), 7.30–7.51 (m, 5H_{arom}).

The residual oil is chromatographed on silica (30 g) eluting with CCl_4, separating **11** 0.10 g (3%) mp 151–153 °C from EtOH (Lit.[22] mp 152–153 °C).

FTIR ($CDCl_3$): ν = 1472, 1487, 1498, 1600, 3034, 3065, 3077 cm^{-1}.

^1H-NMR ($CDCl_3$/TMS): δ = 6.77 (d, 1H, $J_{3,5}$ = 2.0 Hz, (Lit.[22] (CCl_4) δ = 6.62, $J_{3,5}$ = 1.9 Hz), 7.20–7.43 (m, 14H_{arom}), 7.60–7.65 (m, 2H_{arom}).

MS: m/z = 295 (M^+, 100), 191 (38), 77 (38).

This work was supported by the General Electric Company and the Natural Sciences and Engineering Research Council of Canada.

Received: 29 January 1990; revised: 19 April 1990

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