Supplementary Material (ESI) for Chemical Communications

ELECTRONIC SUPPLEMENTARY INFORMATION

Mechanistic Investigation of the Gold-Catalyzed Aerobic Oxidation of Aldehydes: Added Insight from Hammett Studies and Isotopic Labelling Experiments

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Table of Contents

Competition Experiments

In each experiment 2 mmol benzaldehyde was oxidized in competition with 2 mmol of the *para*-substituted benzaldehyde under investigation. Anisol was used as internal standard (1 mmol), and in addition a catalytic amount of base was required (10 mol% NaOH). In each experiment 157 mg gold catalyst (1% wt/wt Au/TiO2, corresponding to a Au:substrate ratio of 1:500) was used, which had been acquired from the World Gold Council (Gold reference catalyst #02-07, Sued-Chemie Catalysts Japan). The reactions were carried in methanol (10 mL) at room temperature in an open system (to allow a supply of air), which was fitted with a reflux condenser to avoid solvent evaporation. Aliquots of 50 μL were withdrawn from the reaction mixture using the following scheme: before addition of catalyst, after addition of catalyst, and then after 5, 10, 15, 30, 45, 60, 90, 120, 150, 180, 240, 300, and 360 mins reaction time, and then diluted with diethyl ether to 1 mL. GC analysis was carried using a Shimadzu GC-2010 system fitted with an Equity-1 column (30m × 0.25mm × 0.25μm) using the following temperature profile: 100 ºC (hold 10 min), then 5 ºC/min to 200 ºC, followed by 10 ºC/min to 300 ºC (hold 5 min).

For the indirect determination of KIE an additional competition experiment was carried out as stated above, where deuterated benzaldehyde was oxidized in competition with *p*-Me-benzaldehyde, which allowed for a straight-forward separation by GC.

The direct determination of KIE was performed as stated above using 2 mmol of both deuterated and normal benzaldehyde. The samples were analyzed using Agilent Technologies 6850 GC coupled to 5975C VL MSD fitted with a HP-5MS column (30 m × 0.25 mm × 0.25). The temperature profile was: 100 ºC (hold 5 min) and then a ramp (40 ºC /min) to 300 ºC. Single ion monitoring was selected (M=105, 106, 107), which allowed the use of the molecular ion of each benzaldehyde to be quantified relative to the molecular ion of the internal standard (anisole, M=105). $^{36}O_2$ (500 mL, 99% isotopic purity) and MeO^{18}H (1 mL, 95% isotopic purity) was acquired from Sigma-Aldrich and used as received. The reactions were carried out in 1 mL of methanol as solvent, and using a balloon to supply the isotopically labelled dioxygen. Samples were withdrawn after 2 hrs, 4 hrs, 8 hrs, and 24 hrs and analyzed by GC-MS in SIM mode (M=136, 137, 138, and 139).

General metods, gas chromatography

Gas chromatography were performed using a Shimadzu GC-2010 system equipped with an autosampler. Method A involved the use of a 30m x 0.25 mm x 0.25 µm Equity-1 column, which were used in conjunction with the following temperature program: 100 ºC (5min), then a ramp (10 ºC/min) to 300 ºC which were kept for 10 mins. Method B involved the use of a 15m x 0.10 mm x 0.10 µm Equity-1 column, which were used in conjunction with the temperature program: 100 ºC (5 min) then a ramp (40 ºC/min) to 300 ºC which were kept for 5 min (so-called FastGC).

Retention Times

Compound	**Method A (30m column)**	**Method B (15m column)**
Anisole	3.37 min	1.59 min
Benzaldehyde	3.78 min	1.79 min
pCH_3-benzaldehyde	5.90 min	2.60 min
pCF_3-benzaldehyde	3.57 min	1.65 min
pCl-benzaldehyde	6.97 min	3.08 min
pOMe-benzaldehyde	12.30 min	6.15 min
pCN-benzaldehyde	10.38 min	4.70 min
pCOOMe-benzaldehyde	16.19 min	7.35 min
Benzaldehyde methyl ester	6.30 min	3.01 min
pCH_3-benzaldehyde methyl ester	10.93 min	4.73 min
pCF_3-benzaldehyde methyl ester	5.85 min	2.58 min
pCl-benzaldehyde methyl ester	12.73 min	5.74 min
pOMe-benzaldehyde methyl ester	17.27 min	7.76 min
pCN-benzaldehyde methyl ester	16.05 min	7.33 min
pCOOMe-benzaldehyde methyl ester	21.15 min	8.49 min

Table 1, entry 1: Benzaldehyde and *para*-cyano-benzaldehyde:

Amounts of reagents used:

	m (mg)
Benzaldehyde	213.5
4-Cyanobenzaldehyde	269.0
Methanol	8026.4
NaOH	17.8
Anisole	119.0
Catalyst (1% Au/TiO_2)	157.5

Areas measured by GC:

Sample no.	Time (min)	Anisol	PhCHO	*p*CN-PhCHO	Conversion PhCHO (%)	Conversion *p*CN-PhCHO (%)
1	0 – no cat.	88759	146551	103154	0.00	0.00
2	0 – after cat.	76986	125093	82212	0.02	0.08
3	5	59419	95225	49707	0.03	0.28
4	10	55630	87791	32823	0.04	0.49
5	15	51040	78794	21625	0.07	0.64
6	30	73452	110337	15636	0.09	0.82
7	45	72099	105269	4236	0.12	0.95
8	60	76552	109162	0	0.14	1.00
9	90	76848	103779	0	0.18	1.00
10	120	91239	114224	0	0.24	1.00
11	150	81553	95109	0	0.29	1.00
12	180	98760	110115	0	0.32	1.00
13	240	45646	40215	0	0.47	1.00
14	300	88253	67387	0	0.54	1.00
15	360	55331	32269	0	0.65	1.00

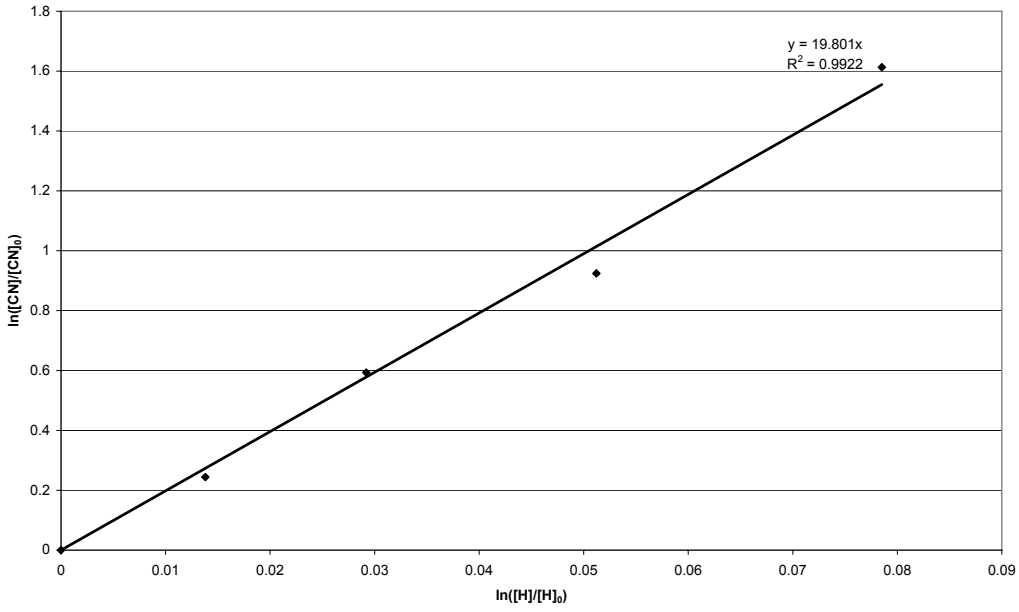


Table 1, entry 2: Benzaldehyde and *para*-(carboxymethyl)-benzaldehyde:

Amounts of reagents used:

	m (mg)
Benzaldehyde	294.2
4-carboxymethyl benzaldehyde	382.4
Methanol	7932.8
NaOH	17.9
Anisole	129.6
Catalyst (1% Au/TiO_2)	157.3

Areas measured by GC:

Sample no.	Time (min)	Anisol	PhCHO	*p*COOMe-PhCHO	Conversion PhCHO (%)	Conversion *p*COOMe-PhCHO (%)
1	0 – no cat.	114277	234070	171396	0.00	0.00
2	0 – after cat.	89659	183156	134345	0.00	0.00
3	5	82138	164663	106449	0.02	0.14
4	10	78745	154472	78059	0.04	0.34
5	15	75360	145409	64333	0.06	0.43
6	30	85961	160636	36907	0.09	0.71
7	45	61807	106727	6165	0.16	0.93
8	60	71782	124611	4865	0.15	0.95
9	90	70603	114216	0	0.21	1.00
10	120	71917	110491	0	0.25	1.00
11	150	89624	129059	0	0.30	1.00
12	180	91772	124050	0	0.34	1.00
13	240	68657	76899	0	0.45	1.00
14	300	106230	99190	0	0.54	1.00
15	360	64979	50089	0	0.62	1.00

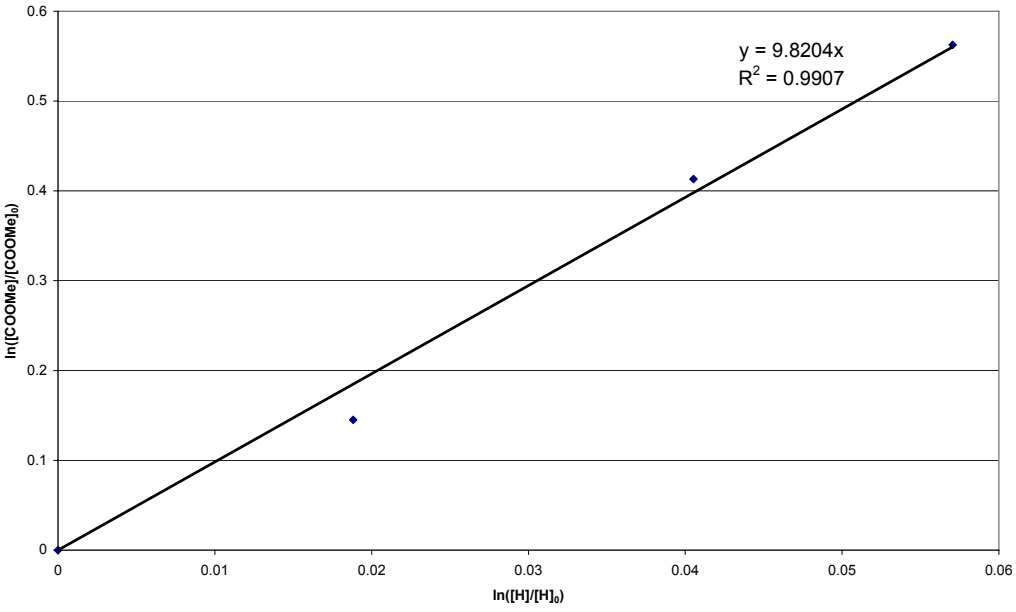


Table 1, entry 3: Benzaldehyde and *para*-chloro-benzaldehyde:

Amounts of reagents used:

	m (mg)
Benzaldehyde	230.4
4-Chloro benzaldehyde	294.1
Methanol	7982.1
NaOH	18.9
Anisole	138.0
Catalyst (1% Au/TiO_2)	157.8

Areas measured by GC:

Sample no.	Time (min)	Anisol	PhCHO	*p*Cl-PhCHO	Conversion PhCHO (%)	Conversion *p*Cl-PhCHO (%)
1	0 – no cat.	109510	167735	160965	0.0	0.0
2	0 – after cat.	120259	183041	172079	0.6	2.7
3	5	78176	115319	101977	3.7	11.3
4	10	72635	103374	89337	7.1	16.3
5	15	106996	148460	121777	9.4	22.6
6	30	110582	145681	112316	14.0	30.9
7	45	65170	83243	60656	16.6	36.7
8	60	90486	114763	84166	17.2	36.7
9	90	78391	96787	66718	19.4	42.1
10	120	85685	104142	69321	20.6	45.0
11	150	95022	112169	75485	22.9	46.0
12	180	85939	98949	62945	24.8	50.2
13	240	97147	107096	62370	28.0	56.3
14	300	62025	64330	34118	32.3	62.6
15	360	74119	73332	36516	35.4	66.5

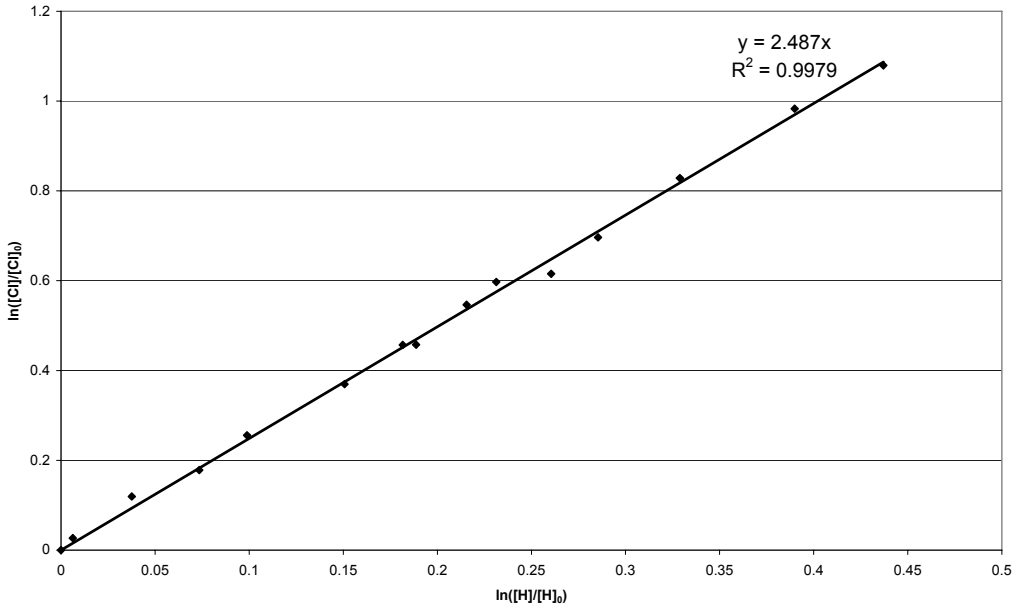


Table 1, entry 4: Benzaldehyde and *para*-(trifluoromethyl)-benzaldehyde:

Amounts of reagents used:

	m (mg)
Benzaldehyde	257.4
4-(Trifluormethyl)benzaldehyd	391.9
Methanol	8096.5
NaOH	17.6
Anisole	115.3
Catalyst (1% Au/TiO_2)	157.7

Areas measured by GC:

Sample no.	Time (min)	Anisol	PhCHO	pCF$_3$-PhCHO	Conversion PhCHO (%)	Conversion pCF$_3$-PhCHO (%)
1	0 – no cat.	48440	98284	106793	0.0	0.0
2	0 – after cat.	74061	149396	158146	0.6	3.1
3	5	55353	105585	112724	6.0	7.6
4	10	86729	162495	165889	7.7	13.2
5	15	69581	124779	128062	11.6	16.5
6	30	41619	69053	69396	18.2	24.4
7	45	43849	70888	68908	20.3	28.7
8	60	56886	89856	86004	22.1	31.4
9	90	54790	84282	78207	24.2	35.3
10	120	53453	81400	73722	24.9	37.4
11	150	40005	57444	52286	29.2	40.7
12	180	45243	64386	56969	29.9	42.9
13	240	40783	55188	47112	33.3	47.6
14	300	49202	65524	52645	34.4	51.5
15	360	69001	86282	66877	38.4	56.0

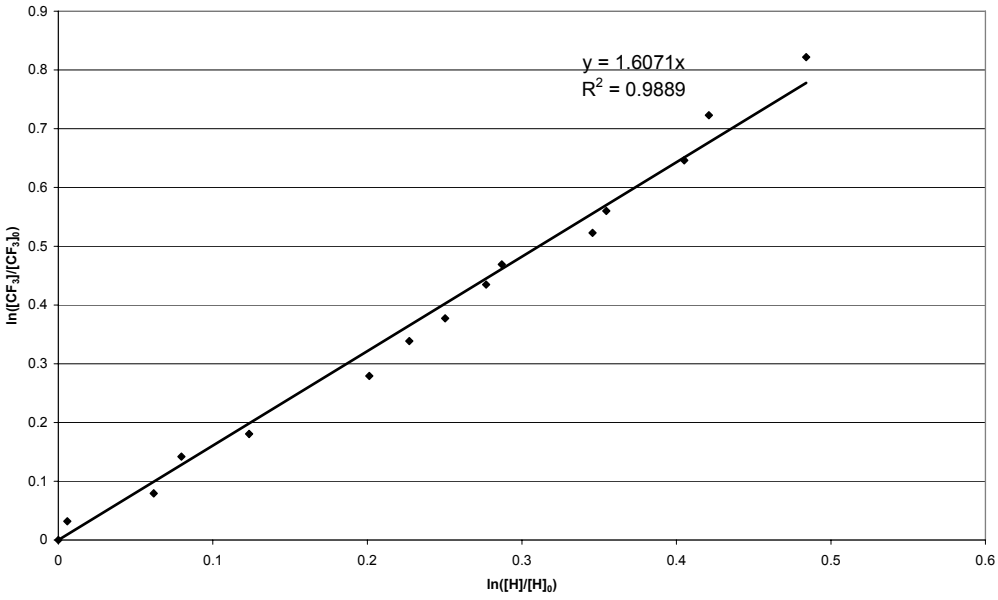


Table 1, entry 5: Benzaldehyde and *para*-methyl-benzaldehyde:

Amounts of reagents used:

	m (mg)
Benzaldehyde	237.2
4-Methyl benzaldehyde	271.1
Methanol	8024.5
NaOH	16.7
Anisole	115.7
Catalyst (1% Au/TiO_2)	157.3

Areas measured by GC:

Sample no.	Time (min)	Anisol	PhCHO	*p*CH_3-PhCHO	Conversion PhCHO (%)	Conversion *p*Me_3-PhCHO (%)
1	0 – no cat.	63024	118297	143482	0.0	0.0
2	0 – after cat.	44404	83274	98405	0.1	2.7
3	5	58344	105702	129164	3.5	2.8
4	10	60997	106298	131017	7.2	5.7
5	15	56016	94265	117431	10.3	7.9
6	30	39868	59853	73216	20.0	19.3
7	45	47481	66864	84623	25.0	21.7
8	60	39520	54223	68254	26.9	24.1
9	90	60533	79586	102753	30.0	25.4
10	120	54204	69031	90578	32.2	26.6
11	150	65246	80547	107285	34.2	27.8
12	180	63651	75584	101644	36.7	29.9
13	240	68848	75811	104574	41.3	33.3
14	300	47635	48178	67082	46.1	38.1

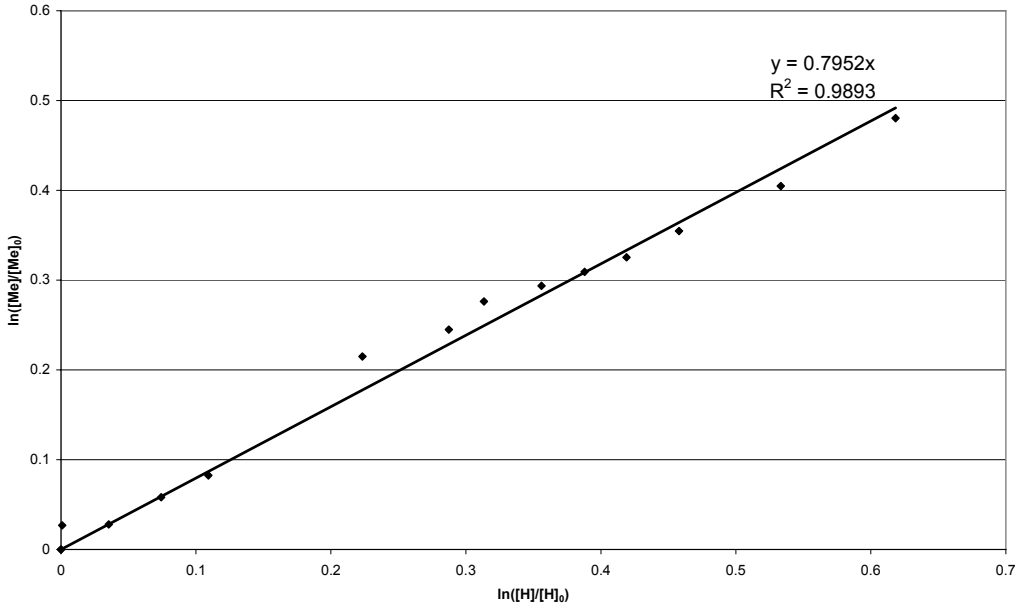


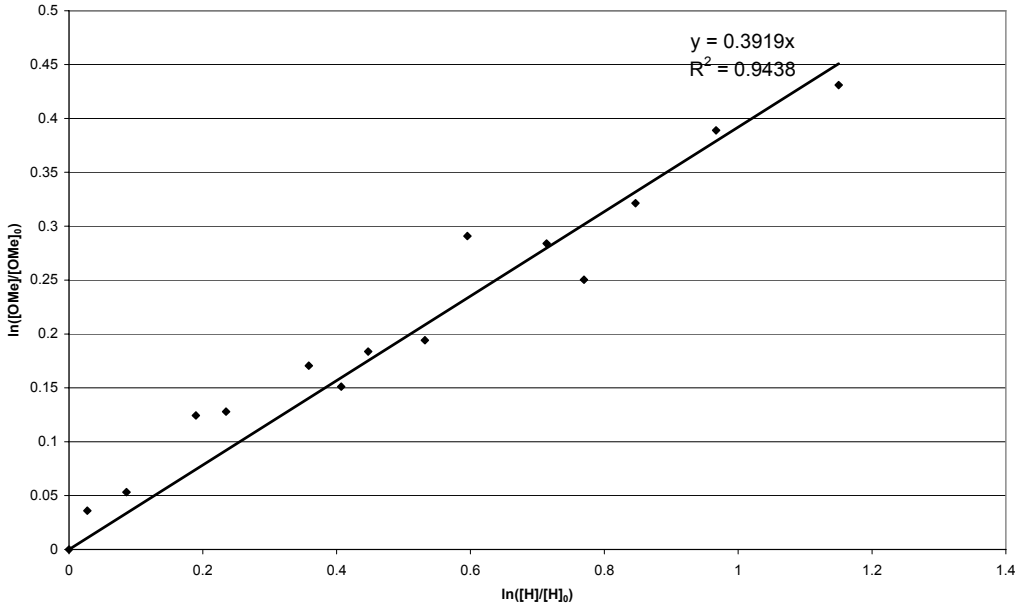
Table 1, entry 6: Benzaldehyde and *para*-methoxy benzaldehyde:

Amounts of reagents used:

	Added amount (mg)
Benzaldehyde	219.5
4-Methoxy benzaldehyde	284.2
Methanol	8458.6
NaOH	19.4
Anisol	139.0
Catalyst (1% Au/TiO_2)	157.5

Areas measured by GC:

Sample no.	Time (min)	Area (GC) Anisol	Area (GC) PhCHO	Area (GC) *p*OMe-PhCHO	Conversion PhCHO (%)	Conversion *p*OMe-PhCHO (%)
1	0 – no cat.	122271	176415	177542	0.0	0.0
2	0 – after cat.	103978	145980	145642	2.7	3.5
3	5	109952	145584	151387	8.2	5.2
4	10	81347	97091	104303	17.3	11.7
5	15	80247	91556	102528	20.9	12.0
6	30	81158	81830	99369	30.1	15.7
7	45	109529	105213	136737	33.4	14.0
8	60	96211	88769	116253	36.1	16.8
9	90	86855	73619	103860	41.3	17.6
10	120	97685	77711	106048	44.9	25.2
11	150	110841	74080	125303	53.7	22.1
12	180	113302	80076	123843	51.0	24.7
13	240	106996	66202	112663	57.1	27.5
14	300	82013	44993	80709	62.0	32.2



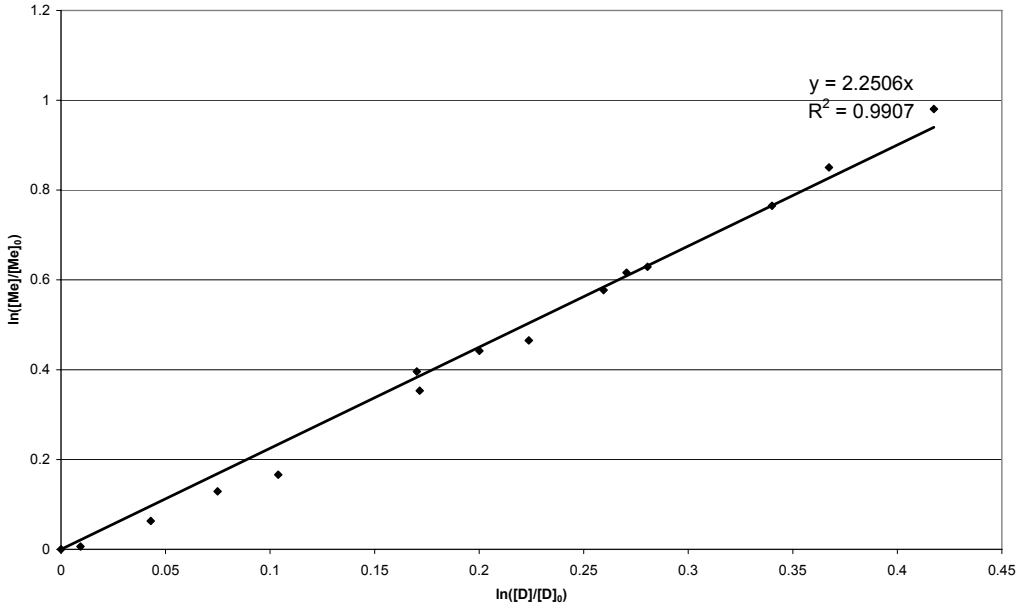
Kinetic Isotope Effect, Indirect Determination: PhCDO vs. *p*Me-PhCHO

Amounts of reagents used:

	Added amount (mg)
d-Benzaldehyde	227.3
4-Methyl benzaldehyde	259.9
Methanol	9246.4
NaOH	18.6
Anisol	113.0
Catalyst (1% Au/TiO_2)	157.9

Areas measured by GC:

Sample no.	Time (min)	Area (GC) Anisol	Area (GC) PhCDO	Area (GC) *p*Me-PhCHO	Conversion PhCDO (%)	Conversion *p*Me-PhCHO (%)
1	0 – no cat.	63329	123916	121622	0.0	0.0
2	0 – after cat.	57577	111617	109877	0.9	0.6
3	5	54357	101891	98001	4.2	6.1
4	10	46813	84990	79025	7.2	12.1
5	15	51842	91428	84313	9.9	15.3
6	30	35874	59210	46372	15.6	32.7
7	45	61141	100777	82480	15.8	29.8
8	60	41299	66154	50972	18.1	35.7
9	90	66943	104727	80740	20.0	37.2
10	120	42704	64460	46042	22.9	43.9
11	150	47653	71146	49425	23.7	46.0
12	180	67616	99944	69228	24.5	46.7
13	240	52135	72604	46586	28.8	53.5
14	300	59971	81274	49208	30.7	57.3
15	360	60755	78305	43775	34.1	62.5



Kinetic Isotope Effect, Direct Determination: PhCHO vs. PhCDO

Amounts of reagents used:

	Added amount (mg)
Benzaldehyde	227.3
d-Benzaldehyde	259.9
Methanol	9246.4
NaOH	18.6
Anisol	113.0
Catalyst (1% Au/TiO_2)	157.9

Areas measured by GC:

Sample no.	Time (min)	Area (MS) Anisol	Area (MS) PhCDO	Area (MS) *p*Me-PhCHO	Conversion PhCHO (%)	Conversion PhCDO (%)
1	0 – no cat.	422446	775025	842560	0.0	0.0
2	0 – after cat.	409387	722321	803709	3.8	1.6
3	5	391750	642686	757165	10.6	3.1
4	10	684540	1017293	1268386	19.0	7.1
5	15	520036	714569	931047	25.1	10.2
6	30	483363	587933	832179	33.7	13.7
7	45	698501	794418	1170985	38.0	15.9
8	60	783373	848936	1288830	40.9	17.5
9	90	469704	467450	751962	45.8	19.7
10	120	874117	807624	1358301	49.6	22.1
11	150	624129	543596	970111	52.5	22.1
12	180	474663	376993	714409	56.7	24.5
13	240	479678	320506	672289	63.6	29.7
14	300	327057	187915	442121	68.7	32.2