Wieland Rearrangement

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Isomerization of Triphenylmethoxyl: The Wieland Free-Radical Rearrangement Revisited a Century Later**

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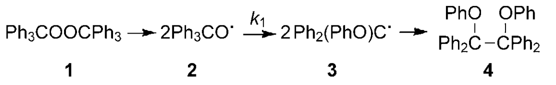
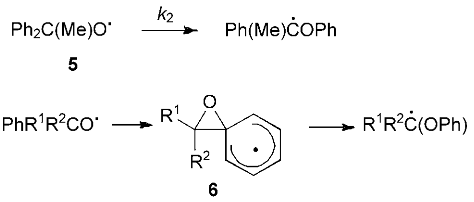
In 1911, Wieland[1] decomposed 20 g (38.6 mmol) of $(Ph_3CO)_2$ (**1**) under CO_2 in boiling xylene for 10 minutes, and separated a crystalline product (13–15 g) by the addition of 70 mL of absolute alcohol and concentration of the crude product. This product was identified as $(Ph_2(PhO)C)_2$ (**4**, 65–75 % yield; Scheme 1). Vacuum distillation (11 mm) of the residue yielded 2.3 g of a yellow oil from which benzophenone (almost 2 g) and phenol (0.2 g) were separated. Further heating gave a substantial, but not quantifiable, amount of Ph_3COH. Wieland's interpretation was that triphenylmethoxyl radicals ($Ph_3CO^\bullet$, **2**) had been formed and had isomerized to $Ph_2(PhO)C^\bullet$ radicals (**3**) which then coupled (Scheme 1). This was the first clearly demonstrated, and explicitly shown, free-radical rearrangement—a priority often overlooked.



$$\underset{\mathbf{1}}{Ph_3COOCPh_3} \rightarrow \underset{\mathbf{2}}{2Ph_3CO^\bullet} \xrightarrow{k_1} \underset{\mathbf{3}}{2\,Ph_2(PhO)C^\bullet} \rightarrow \underset{\mathbf{4}}{Ph_2\overset{PhO}{C}-\overset{OPh}{C}Ph_2}$$

Scheme 1. Rearrangement of triphenylmethoxyl (**2**).

The rate constants and mechanisms of isomerization of triphenylmethoxyl (**2**)[2–4] and the analogous isomerizations of $Ph_2C(Me)O^\bullet$ (**5**),[2–10] and related radicals (Scheme 2),[7–12] have received considerable attention. Claims that discrete spiro intermediates (**6**) had been identified in the rearrangements of **2**[3] and **5**[2,3] have been disproven.[4,6] However, computational studies on the rearrangement of **5**[9,10] (and $PhCH_2O^\bullet$)[11] do indicate stepwise processes with spiro radicals (**6**) as intermediates (Scheme 2). Consistent with these calculations, cumyloxyl radicals, $PhC(Me)_2O^\bullet$, *para* substituted with a 2,2-diphenylcyclopropyl reporter group, have been demonstrated to be in equilibrium with spiro radicals **6**.[12]



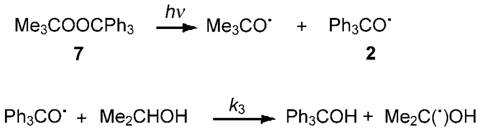
Scheme 2. Formation of oxaspiro intermediates, **6**.

Rate constants ($10^{-6} \times k_2\,s^{-1}$) measured at room temperature by laser flash photolysis (LFP) in CH_3CN were 2.5,[6] 2.8,[7,8] and 3.2 s^{-1},[2] and are nicely bracketed by the result of density functional theory (DFT) calculations ($10^{-6} \times k_2\,s^{-1}$ = 0.93[9] and 7.9 s^{-1}[10]). Experiment[8] and theory[9,10] agree that k_2 depends on the nature of the *para* substituent. In addition, k_2 decreases as solvents become more polar.[8] In contrast, the rate of β scission of the cumyloxyl radical increases in more polar solvents (Scheme 3).[13]

$$PhC(Me_2)O^\bullet \longrightarrow PhC(O)Me + Me^\bullet$$

Scheme 3. β Scission of the cumyloxyl radical.

The only previous experimental study of the kinetics of the rearrangement of **2** to **3** was carried out by Schuster et al.,[2] who relied on the photolysis of $Me_3COOCPh_3$ (**7**) to generate **2** (Scheme 4). Picosecond LFP (266 nm) of **7** in CH_3CN gave a broad absorption signal (λ_{max} = 545 nm) attributed to **3** that appeared within the 17 ps width of the laser pulse and persisted for at least 6 ns.[2] The authors[2] concluded that k_1 exceeds $5 \times 10^{10}\,s^{-1}$. Furthermore, photolysis of **7** at 254 nm in *i*PrOH saturated with N_2 gave dimer **4**, benzophenone, and phenol, but no (< 0.5 %) Ph_3COH.[2] Assuming that k_3 is approximately equal to the $Me_3CO^\bullet$ +



$$\underset{\mathbf{7}}{Me_3COOCPh_3} \xrightarrow{h\nu} Me_3CO^\bullet + \underset{\mathbf{2}}{Ph_3CO^\bullet}$$

$$Ph_3CO^\bullet + Me_2CHOH \xrightarrow{k_3} Ph_3COH + Me_2C(^\bullet)OH$$

Scheme 4. Photolysis of peroxide **7**.

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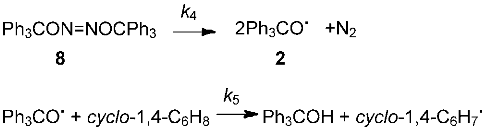
Me_2CHOH rate constant ($1.8\times10^6\,\text{M}^{-1}\,\text{s}^{-1}$)[14] the lower limit for k_1 in neat *i*PrOH (13 M) is $\approx(1.8\times10^6\times13)/0.005=(2.3\times10^7)\times200=5\times10^9\,\text{s}^{-1}$, a result consistent with the LFP experiment.

The reported[2] absence of Ph_3COH[15] and presence of benzophenone led us to suspect (see the Supporting Information) that UV photolysis of compound **7** did not give **2** in its ground state and to doubt that k_1 is larger than $5\times10^{10}\,\text{s}^{-1}$. We therefore redetermined k_1 using **2** generated thermally in the presence of hydrogen-atom donating solvents.

The most convenient, room temperature, thermal source of **2** seemed likely to be hyponitrite **8** (Scheme 5).[16]



$$\underset{\mathbf{8}}{Ph_3CON{=}NOCPh_3} \xrightarrow{k_4} 2\underset{\mathbf{2}}{Ph_3CO^\bullet} + N_2$$

$$Ph_3CO^\bullet + \textit{cyclo}\text{-}1,4\text{-}C_6H_8 \xrightarrow{k_5} Ph_3COH + \textit{cyclo}\text{-}1,4\text{-}C_6H_7^\bullet$$

$$k_1 = (1\text{-}f)\,k_5[\textit{cyclo}\text{-}1,4\text{-}C_6H_8] \qquad (1)$$

Scheme 5. Hyponitrite route to triphenylmethoxyl (**2**).

Thermolysis of **8** in CH_2Cl_2 in air at 295 K ($k_4^{295\,\text{K}}=1.1\times10^{-4}\,\text{s}^{-1}$, see the Supporting Information) with periodic analyses by HPLC (see Table S1 and Figure S1 in the Supporting Information) and (after complete decomposition of compound **8**) analyses by GC and GC/MS, showed that the main products were **4** (by comparison with authentic **4**, which is unstable in solution, see the Supporting Information), phenol, benzophenone, and a minor amount of $PhCO_2Ph$.[17] Samples collected after reaction times of 67×10^3 seconds and 486×10^3 seconds contained $\approx$9.5 % of **1**,[18] which is stable at 295 K. Identified species (unchanged **8** and its products) accounted for approximately 100 % of the phenyl groups for up to 11×10^3 seconds (see the Supporting Information).

In the absence of air, **8** was thermolysed in solvent mixtures containing CH_2Cl_2 (to solubilize **8**) and the hydrogen atom donor, 1,4-cyclohexadiene. HPLC analyses showing the loss of **8** and formation of products are presented for 1,4-C_6H_8/CH_2Cl_2 (80:20, v/v), in the Supporting Information. The main product was Ph_3COH, which would not have been detected if k_1 were $5\times10^{10}\,\text{s}^{-1}$ or larger. Other lesser products (see the Supporting Information) included $Ph_2(PhO)CH$, two compounds resulting from combinations with 1,4-C_6H_8, minor amounts of **2** (at short reaction times), and (after 624×10^3 s) 2.6 % of **1**. Triphenylmethanol was also formed with lower 1,4-C_6H_8/CH_2Cl_2 ratios (see the Supporting Information). The yield of freely diffusing **2** will be $2\times[(\mathbf{8}_0-\mathbf{8}_t)-\mathbf{1}_t]$ or, after complete decomposition of compound **8**, $2\times(\mathbf{8}_0-\mathbf{1}_{\text{final}})$. Based on the 2.6 % yield of **1**, the minor correction for in-cage combination of geminate **2** will be assumed to be a constant 2.5 % of decomposed **8**. Thus, the yield of free **2** during the reaction is $2\times0.975\times(\mathbf{8}_0-\mathbf{8}_t)$, with a final yield of $2\times0.975\times\mathbf{8}_0$. It is only some fraction of **2**, $f=Ph_3COH/[1.95\times(\mathbf{8}_0-\mathbf{8}_t)]$, that can form Ph_3COH (Scheme 5), while the remaining, 1-*f*, fraction of these radicals will isomerize and form other products. This competition yields k_1 via Equation (1). Again assuming that k_5 will be essentially equal to the $Me_3CO^\bullet$ + 1,4-C_6H_8 rate constant, that is, $4\times10^7\,\text{M}^{-1}\,\text{s}^{-1}$, see the Supporting Information, the mean value of $k_1^{295\,\text{K}}$ (derived from several experiments, see Supporting Information) was $1.4\times10^8\,\text{s}^{-1}$.

We next repeated Wieland's experiment. As the purity and water content of his "xylene" are unknown, **1** was decomposed at 411 K in: 1) 1.2 mL of dry *m*-xylene at reflux, 2) as in 1) but water saturated, and 3) as in 1) but using EtOH[1] in the work-up procedure. After **1** (0.099 mmol) had completely decomposed (10 min, as evident by HPLC), solutions were diluted to 10 mL with CH_3CN (1 and 2) or EtOH (3) and analyzed by GC. Ph_3COH was present in low, but equal, yields in these three experiments (see the Supporting Information). As each molecule of **1** gives two $Ph_3CO^\bullet$ (**2**), the yields of alcohol indicated that 1.34 % of the triphenylmethoxyl (**2**) has abstracted hydrogen from the xylene, Scheme 6, and that the other 98.66 % must have isomerized. A value for $k_6^{411\,\text{K}}=4\times10^6\,\text{M}^{-1}\,\text{s}^{-1}$ was estimated from room temperature kinetic data (see the Supporting Information) which was combined with the Ph_3COH yield and the molarity of neat *m*-xylene at 411 K (7.1 M) to give $k_1^{411\,\text{K}}=(4\times10^6\times7.1)/0.0134=2.1\times10^9\,\text{s}^{-1}$.

$$Ph_3CO^\bullet + m\text{-}C_6H_8\,(CH_3)_2 \xrightarrow{k_6} Ph_3COH + m\text{-}C_6H_4\,(CH_3)CH_2^\bullet$$

Scheme 6. Wieland's experiment (formation of Ph_3COH).

Combination of $k_1^{295\,\text{K}}=1.4\times10^8\,\text{s}^{-1}$ with $k_1^{411\,\text{K}}=2.1\times10^9\,\text{s}^{-1}$ would yield a two point Arrhenius plot, $E_{a1}=5.6$ kcal mol^{-1}, $\log(A_1\text{s}^{-1-1})=12.3$ (for a discussion of the "expected" value of A_1 see the Supporting Information). We also applied DFT[19] to **2**. Phenyl migration was again found to proceed via a spiro intermediate, **6** (Figure 1 a), that lies in a shallow energy minimum. Relative free enthalpies (at 298 K in kcal mol^{-1}) along the reaction coordinate corresponding to the isomerization of **2** are: reactant, 0.0; transition state (TS) #1 (O approach to C1 of Ph), 5.7; intermediate **6**, 5.2; TS #2 (opening of the 3-membered ring), 5.5; final product, –20.8 (see Figure S3 in the Supporting Information). More interestingly, $k_1^{295\,\text{K}}$ was computed to be $2.0\times10^8\,\text{s}^{-1}$, with log ($A_1\text{s}^{-1}$) = 12.9 and $E_{a1}=6.2$ kcal mol^{-1} calculated over the

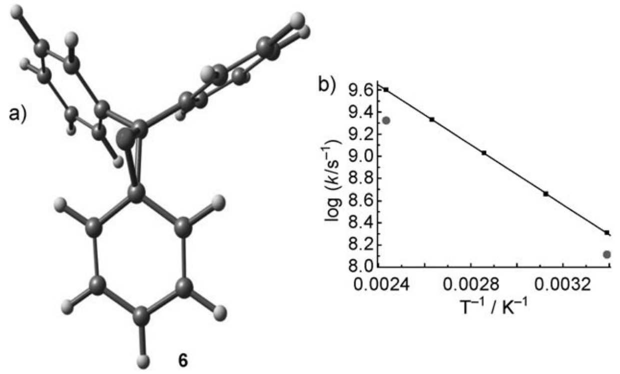
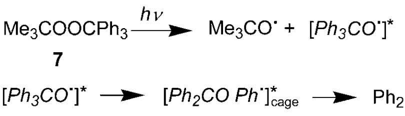


Figure 1. a) View of the spiro intermediate **6**, predicted by DFT for the isomerization of **2**. b) Isomerization of **2**, Arrhenius plot calculated by DFT (■) and two experimental rate constants (●).

temperature range 295–411 K. These results are in very good agreement with experiment, see Figure 1 b.

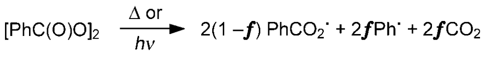
Schuster et al.[2] reported that Ph_3COH was not produced ($< 0.5\,\%$) during photolysis of **7** at 254 nm under N_2 in neat *i*PrOH, a result that is inconsistent with $k_1^{295\,K} = 1.4 \times 10^8\ s^{-1}$ (taking $k_3[iPrOH] = 2.3 \times 10^7\ s^{-1}$, see above). Complete thermal decomposition of **8** (3.30 mmol) in *i*PrOH (6.55 M in CH_2Cl_2, the latter required for solubility) at 295 K gave 0.682 mmol of Ph_3COH, a yield of 10.6 % (based on two molecules of **2** formed per **8**, see above). This translates to $k_1^{295\,K} = 1.05 \times 10^7\ s^{-1}$ which is only about 8 % of the value in 1,4-C_6H_8/CH_2Cl_2. As the rate constants used for the two competing hydrogen-abstraction reactions come from the same technique (and source),[14] the rate of isomerization of **2** must be solvent dependent.[20]

All the results presented above prove that UV photolysis of $Me_3COOCPh_3$ (**7**) does not yield significant amounts of triphenylmethoxyl (**2**) in its ground state. Instead, photolysis must yield $Ph_3CO^\bullet$ in an excited state, $[Ph_3CO^\bullet]^*$, and, before this "cools" to its ground state, it undergoes unimolecular decomposition with $k > 5 \times 10^9\ s^{-1}$ (see above, not necessarily with $k > 5 \times 10^{10}\ s^{-1}$, see below). Benzophenone formation[2] implies that some "hot" $Ph_3CO^\bullet$ undergoes β scission (Scheme 7).[21]



Scheme 7. Excited state radical formation.

Production of excited $Ph_3CO^\bullet$ by UV photolysis of peroxide **7** is plausible because the Ph_3C group will absorb $> 99\,\%$ of the UV energy and the O–O bond $< 1\,\%$, as was recognized by Schuster et al.,[2] who nevertheless presumed a "rapid intramolecular energy transfer" followed by "oxygen–oxygen bond rupture". A difference in the behavior of thermally and photochemically produced radicals was first reported by Bevington and Lewis[22] who showed that the thermal decomposition of benzoyl peroxide (labeled with ^{14}C in the carboxylate positions) yielded benzoyloxyl radicals exclusively (Scheme 8, $f = 0$), whereas photolysis gave both $PhCO_2^\bullet$ and $Ph^\bullet$ ($f = 0.29$). The $PhCO_2^\bullet$ that survived photogeneration behaved in the same way as the thermally generated $PhCO_2^\bullet$, and presumably came from the PhC(O)O half of the molecule that did not absorb the incident photon—a presumption consistent with the significantly smaller $PhCO_2$/$Ph^\bullet$ ratio in photolyzed *tert*-butyl perbenzoate.[23] Ironically, even if Schuster et al.[2] had generated **2** in the ground state it is improbable that it could have been unambiguously detected, even by picosecond LFP, because the broad absorption of $Ph_2(PhO)C^\bullet$ will differ only marginally from the broad absorption of $Ph_3CO^\bullet$.[24]



Scheme 8. Benzoyl peroxide homolysis.

Wieland's identification of the first free-radical rearrangement did not rely on modern instrumentation but on careful product analyses by classical methods and inspired chemical insight. We take this opportunity to pay homage to this outstanding organic chemist.[26,27]

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Keywords: peroxide · radical reactions · reaction kinetics · rearrangements

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[15] Reference [2] misses Wieland's[1] identification of Ph_3COH and states: "this radical ($Ph_3CO^\bullet$) rearranges to the phenoxydiphenylmethyl radical to the exclusion of hydrogen atom abstraction reactions" with a citation to Wieland!.
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[17] In the presence of oxygen, benzophenone and phenyl benzoate will be formed by the reaction cascade: $Ph_2(PhO)C^\bullet + O_2 \rightarrow\rightarrow Ph_2(PhO)CO^\bullet \rightarrow Ph_2CO + PhO^\bullet$ $Ph_2(PhO)CO^\bullet \rightarrow (PhO)_2(Ph)C^\bullet \rightarrow O_2 \rightarrow\rightarrow (PhO)_2(Ph)CO^\bullet \rightarrow PhC(O)(OPh) + PhO^\bullet$.
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[21] The photolysis in 2-propanol yielded[2] "the product normally assumed to be the $[Ph_2(PhO)C^\bullet]$ dimer" possibly via an in-cage collapse of the (still "hot") products, see Scheme 7 i.e., $[Ph_2CO\ Ph^\bullet]^*_{cage} \rightarrow Ph_2(PhO)C^\bullet$.
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