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Esters of Pyromellitic Acid. Part I. Esters of Achiral Alcohols: Regioselective Synthesis of Partial and Mixed Pyromellitate Esters, Mechanism of Transesterification in the Quantitative Esterification of the Pyromellitate System Using Orthoformate Esters, and a Facile Synthesis of the Ortho Pyromellitate Diester Substitution Pattern

John B. Paine III*

Philip Morris U.S.A., Research Center, P.O. Box 26583, Richmond, Virginia 23261

John.B.Paine@pmusa.com

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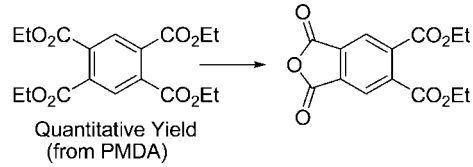

Mild conditions and reversible anhydride formation allow a relative differentiation to be made of the four equivalent carbonyl groups of pyromellitic dianhydride (PMDA, benzene-1,2,4,5-tetracarboxylic dianhydride) in esterification, leading to regioselective methods to generate a wide range of partially or totally esterified products or products bearing differing esterifying groups at the different positions. Pyromellitate monoester anhydrides form efficiently in dichloromethane/triethylamine from 1 equiv of the alcohol. Under the same conditions, two *different* alcohols can be made to react sequentially. With 2 equiv of an alcohol, the usual mixture of meta and para diesters is obtained, separated by crystallization from HOAc. Meta and para dibenzyl pyromellitates served as regiospecific sources of other diesters, by further esterification followed by hydrogenolysis. Refluxing orthoformate triesters were found to effect *quantitative* esterification of the pyromellitate system under autocatalytic conditions; minor ester exchange with pre-existing esters (0−5% of total product) was ascribed to reversible anhydride formation. For general esterification with alcohols, partial ester acid chlorides were obtained using oxalyl chloride. Pyromellitate triesters afforded the ortho diester anhydrides upon distillation, thereby providing facile entry into the mostly novel ortho substitution pattern in this system. The requisite triesters were prepared by selective saponification or by the prior incorporation of one benzyl ester substituent, which could be removed by catalytic hydrogenolysis. The various benzyl esters of pyromellitates hydrogenolyzed smoothly to release the carboxylic acid groups without disturbance of pyromellitate aromaticity.

Introduction

Pyromellitic dianhydride (PMDA) (1*H*,3*H*-benzo[1,2-*c*:4,5-*c*′]difuran-1,3,5,7-tetrone or benzene-1,2,4,5-tetracarboxylic dianhydride) (**1**) is of commercial importance for the production of specialty polymers[1] (e.g., polyimides) and plasticizers.[2] Despite the importance and ready availability of **1** (several thousand tons per annum worldwide[1] and growing), the reported chemistry of PMDA or of pyromellitic acid has been remarkably sparse, particularly outside the context of polymers. The tetramethyl (**4a**) and tetraethyl (**4b**) esters have been known since before the first edition of Beilstein,[3] but the first partial esters did not appear in the literature[4] until the advent of NMR allowed definite structural assignment of the products.

Interest here arose in the pyromellitate system while novel resolving agents were being sought, and it was decided to react PMDA with (l*R*,2*S*,5*R*)-(−)-menthol. The chemistry of a wide range of chiral derivatives of pyromellitic acid[5] and of other

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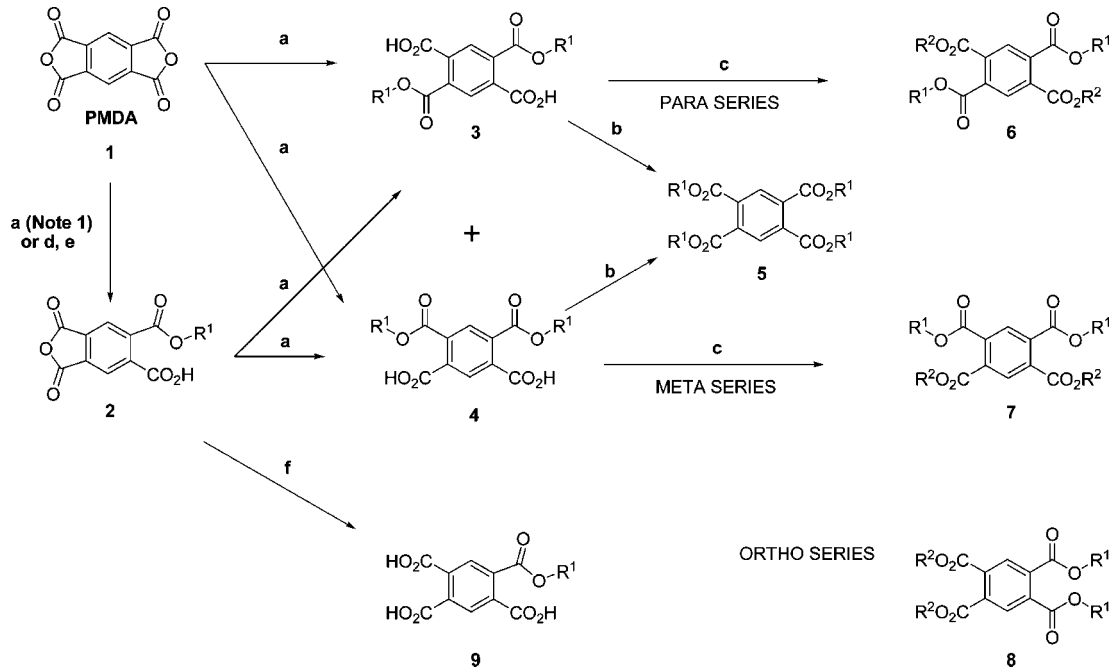
SCHEME 1. Alcoholysis of PMDA (1) and Further Esterification of Pyromellitate Diesters with Orthoformates; Illustration of the Trivial Nomenclature[a]



[a] Compound numbering for **2**−**8**: "a" series, R^1 = Me, R^2 = Et; "b" series, R^1 = Et, R^2 = Me. Reagents and conditions: (a) R^1OH, reflux; (b) $HC(OR^1)_3$, reflux; (c) $HC(OR^2)_3$, reflux; (d) R^1OH, Et_3N/CH_2Cl_2; (e) HCl; (f) H_2O/HOAc. Note 1: if en route to **3** and **4**.

aromatic polycarboxylic acids[6] constitutes the subject of the following paper and another in preparation. Here, attention will be confined to the achiral partial and mixed esters of pyromellitic acid that were prepared in the course of modeling the chemistry to be applied to chiral analogs. It was found that the unique features of symmetry and topology of the PMDA system allowed a considerable relative differentiation to be made among the four carbonyl groups. This allowed a wide range of regiospecific products to be prepared efficiently in a readily isolated and purified form. Of importance to the success of this work was the development of a mild but efficient esterification method for the pyromellitate system that minimized transesterification of pre-existing esters.

To simplify the following discussion, a trivial nomenclature will be adopted that is appropriate to the topology of the benzene-1,2,4,5-tetracarboxylate system. Pyromellitate derivatives containing one or two *pairs* of identical substituents can be conveniently referred to as "ortho" (e.g., **8** or **12**), "meta" (e.g., **4** or **7**), or "para" (e.g., **3** or **6**), in reference to the respective relative relationships held by the identical substituents.

Results and Discussion

Alcoholysis of PMDA (1) to Monoesters and Diesters. The autocatalyzed alcoholysis of PMDA (**1**) in excess alcohol has been shown to give the expected mixture of para (**3**) and meta (**4**) diesters (Scheme 1),[4,7–11] separated by chromatography or fractional crystallization.

In general, the para diesters (**3**), functional derivatives of terephthalic acid, have been found both here and elsewhere to be less soluble and more easily isolated than their meta analogs (**4**), derivatives of isophthalic acid. Evidently the two isomer series show only a slight tendency to mutual solid solution, since even the crude first crops of the para diesters have been found here to be usually isomerically pure, as observed by NMR. The wide melting range reported[9] for para dimethyl pyromellitate (**3a**), which was attributed to isomeric impurity, was more likely due to a decomposition of the material upon fusion. Pyromellitate diesters do not melt reversibly or sharply if at temperatures above ca. 200 °C, regardless of purity, due to the onset of pyrolytic decomposition involving anhydride formation. For both ^1H and ^{13}C NMR, the meta and para diesters are easily distinguished. C-3 and C-6 and their appended protons are chemically and magnetically equivalent for the "para" (and "ortho") isomers, but distinct for the "meta" isomers.

To achieve the efficient formation of pyromellitate *monoesters* (e.g., **9**), the supply of reacting alcohol has to be restricted to 1 equiv. PMDA (**1**) is nearly insoluble in dichloromethane, or in CH_2Cl_2 containing either stoichiometric alcohol (primary or secondary) or triethylamine. However, it was found to dissolve violently when *both* are present in stoichiometric amounts, bringing the solvent to a boil at the concentrations typically used. (In practice, it became usual to add the amine gradually to a mixture of the other ingredients.) With 2 equiv of reagents,

(2) (a) Stozhkova; G. A.; Bondarenko, A. V.; Farberov; M. I.; Priborets, V. M. *Uch. Zap. Yarosl. Tekhnol, Inst.* **1969**, *11*, 185–192. (CA 75: 64779s). (b) Sung, C-K.; Lee, D. C.; Shin, D. K. *Haksurwon Nonmunjip, Cha'yon Kwahak P'yon* **1974**, *13*, 9–15. (CA 84: 136493e). (c) Nanu, I.; Tolan, M.; Coseriu, C. *Mater. Plast. (Bucharest, Rom.)* **1975**, *12*, 138–142. (CA 84: 181040r).

(3) Beilstein, Vol. 9, 997−998 (System Number 1025).

(4) Jones, J. I.; Ochynski, F. W.; Rackley, F. A. *Chem. Ind. (London)* **1962**, 1686–1688.

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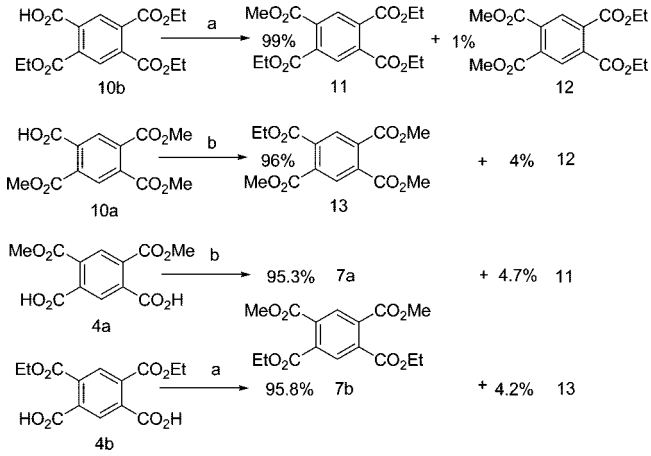
(10) Nishizaki, S.; Moriwaki, T. *Kogyo Kagaku Zaashi* **1968**, *71*, 1559.

(11) Ueda, M.; Takahashi, M.; Hishiki, S.; Imai, Y. *J. Polym. Sci. Polym. Chem. Ed.* **1979**, *17*, 2459–2468.

SCHEME 2. Products and Ester-Exchanged Byproducts Noted from the Reaction of Pyromellitate Partial Esters with Trialkyl Orthoformates[a]



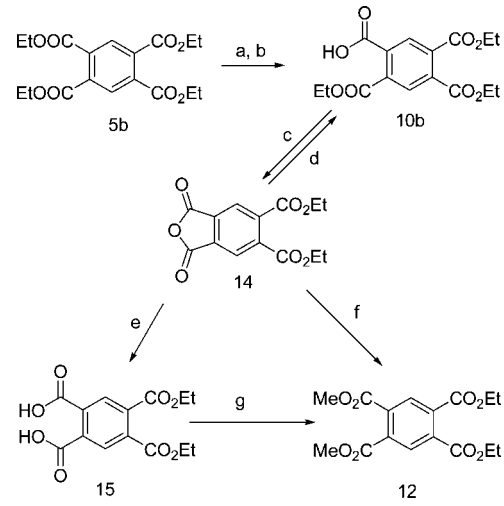
[a] Reagents: (a) $HC(OMe)_3$; (b) $HC(OEt)_3$.

this boiling was observed to continue for some time after the solution became homogeneous (a fact more obvious with larger scale reactions), suggesting that the second anhydride ring to react was significantly less reactive than the first. Thus, subsequently, when *only 1 equiv* of an alcohol was used, a homogeneous reaction mixture was also found to result, and pyromellitate monoesters (e.g., **9**, Scheme 1 or **17**, Scheme 4) could be obtained in good yield upon workup.

A significantly greater reactivity of the first-reacting anhydride ring of **1** relative to that remaining on the intermediary triethylammonium salt of the pyromellitate monoester anhydride (e.g., the Et_3NH^+ salt of **2**) is consistent with a report[12] on the kinetics of the *hydrolysis* of PMDA (**1**): the first anhydride ring to react reportedly did so at a rate of about 20 times faster than the second one. Previous syntheses of monoesters had tended to use great excesses of PMDA in pyridine[13,14] or particular solvents such as dioxane.[15] A study had also been made of ester formation from PMDA in the presence of *aqueous* alcohols.[16]

With 2 equiv of an alcohol, however, the two diesters (**3** and **4**) were formed. These could be isolated by acidification of the triethylammonium salts with HCl and separated by fractional crystallization. For products derived from sufficiently bulky esterifying alcohols, such as benzyl (Scheme 5), a particularly good solvent system for effecting fractional crystallization proved to be acetic acid−H_2O. The para diester (**3** or **21**) could be obtained first from glacial acetic acid; the meta diester (**4** or **22**) usually crystallized upon aqueous dilution of the filtrates. The meta to para ratios under the various conditions appear to fall somewhere in the range of 40:60 to 60:40 as estimated by NMR and display no obvious correlation to the reaction conditions. A detailed study was not made of this point. A recent study used HPLC to determine a slight preference for the formation of the meta diester (**4a**)[17] from PMDA (**1**) and methanol. This result may have been concentration-dependent,

SCHEME 3. Synthesis of Ortho Diethyl Pyromellitate Anhydride (14) by Pyrolysis of Triethyl Pyromellitate (10b) and Further Transformations of 14[a]



[a] Reagents and conditions: (a) NaOH, H_2O, EtOH, rt; (b) HCl; (c) pyrolysis/distillation, >180 °C, loss of EtOH; (d) EtOH, reflux; (e) H_2O, HOAc, reflux; (f) MeOH, $HC(OMe)_3$, reflux; (g) $HC(OMe)_3$, reflux.

since under concentrated preparative conditions, where the acidity is higher than obtained at high dilution, more favorable proportions of the para isomer appear to result; here, an isolated yield of 55% of the para dimethyl ester (**3a**) was obtained.

Pyromellitate Tetraesters. To esterify the pyromellitate system beyond the diester stage has generally required conditions that were harsh (prolonged reflux of alcoholic solutions with mineral acids[18] or acylization in concentrated H_2SO_4 followed by alcoholic quenching[19]), undesirable (reagents such as diazomethane or dimethyl sulfate), or impractical[3] (silver salts, alkyl iodides). Such conditions as the Fischer−Speier synthesis do not lend themselves to selectivity or differentiability within the pyromellitate system and give only moderately high yields. A reported[20] esterification of pyromellitic acid involving the use of tertiary amines and *p*-toluenesulfonyl chloride as condensing reagents for alcohols appears to be of limited preparative value. Pyromellitate partial esters had been reportedly[21] esterified further by reaction with olefins under catalysis by boron trifluoride etherate.

Esterification with Orthoformate Esters. It has been found here that refluxing orthoformate esters[22a,b] (triethyl or trimethyl), *taken in permanent excess*, effect *quantitative* esterification of the pyromellitate system within a few hours (Scheme 1). Depending on the choice of orthoformate ester, the various pyromellitate partial esters (such as **3** or **4**) are converted to tetraesters (**5**) or regiospecific para or meta bis-diesters (**6** or **7**, respectively). PMDA (**1**) reacts directly with mixtures of orthoformate esters and the corresponding alcohol to give the

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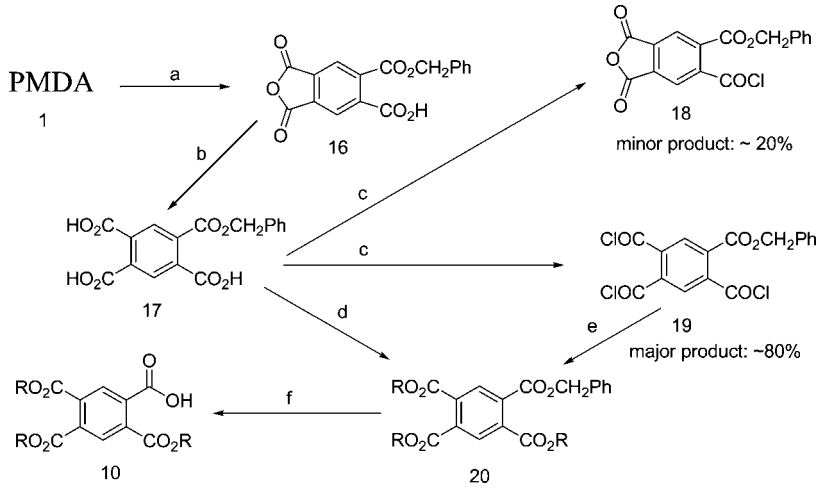
(22) (a) Cohen, H.; Meier, J. D. *Chem. Ind. (London)* **1965**, 349–350. (b) Paine, J. B. *J. Heterocyclic Chem.* **1987**, *24*, 351–355. (c) Hosangadi, B. D.; Dave, R. H. *Tetrahedron Lett.* **1996**, *37:35*, 6375–6378.

SCHEME 4. Benzyl-ester Assisted Synthesis of Pyromellitate Triesters (10)[a]



[a] Numbering for compounds **10** and **20**: "a" series, R = Me; "b" series, R = Et. Reagents and conditions: (a) $PhCH_2OH$, Et_3N, CH_2Cl_2, rt to reflux; HCl/CH_2Cl_2 workup; (b) H_2O, HOAc, brief reflux; (c) $(-COCl)_2$, CH_2Cl_2, catalytic $HCONMe_2$, reflux; (d) $HC(OR)_3$, reflux; (e) ROH, Et_3N, CH_2Cl_2, rt; (f) H_2, Pd−C, THF, 1 atm, rt.

tetraesters (**5**) essentially quantitatively under "single pot" conditions. The reaction is complete when low-boilers (the alcohol and corresponding formate ester) cease forming, and the boiling point of the excess orthoformate ester is permanently observed in the refluxing vapors. Since no extraneous catalyst is required (or even desirable),[22a] workup is a simple matter of distillation, first to recover the unused reagent and then to recover the product (**5**). Due to the vast disparity in vapor pressure between orthoformate reagent and pyromellitate tetraester, even a Kugelrohr can effect total separation of the pair. The traces of nonvolatile residue left after distillation could be ascribed to impurities in the PMDA (**1**), since pure partial esters afforded no residue when esterified further with orthoformate and then distilled. The consumption of orthoformate ester in the reaction was close to the theoretical of 2 molar equiv per mole of PMDA (**1**). Traces of water in the alcohol used, minor losses of reagent vapor to the removed low-boilers, or prior hydration of some of the PMDA (**1**) would account for the minor excess consumption of reagent. The pyromellitate tetraesters are impervious to orthoformate esters, which are therefore taken in excess to ensure that the esterification process is driven to completion.

A most significant feature of the reaction, both from a mechanistic standpoint and from the angle of practical synthesis, is that little if any exchange (e.g., <5% of the total product) appears to occur between the orthoformate ester and esters already present on the pyromellitate system, *under the recommended uncatalyzed conditions*. Thus, a pure sample of para dimethyl pyromellitate[7,9] (**3a**) was converted to para dimethyl diethyl pyromellitate (**6a**) in boiling triethyl orthoformate. The homogeneity of the recrystallized product was readily confirmed by both NMR and GC/MS. By similar means, reasonably pure (95+%) samples of the meta (**7a** = **7b**) and ortho (**12**) diethyl dimethyl pyromellitates and the triethyl methyl (**11**) and ethyl trimethyl (**13**) esters were also obtained. [These were of some interest to see to what extent NMR (^1H or ^{13}C) could distinguish such subtleties as the differential effects of carbomethoxy versus carboethoxy substitution. Such differences can be seen by inspecting the tables included in the Supporting Information. More importantly, the availability of all three dimethyl diethyl pyromellitate isomers was helpful in elucidating the mechanism of the minor observed transesterification, discussed below.] Only a limited number of pyromellitate mixed esters have been reported to date, usually without explicit isomer attribution. These include dibutyl di-2-octyl pyromellitate[21] and dimethyl diethyl pyromellitate.[23]

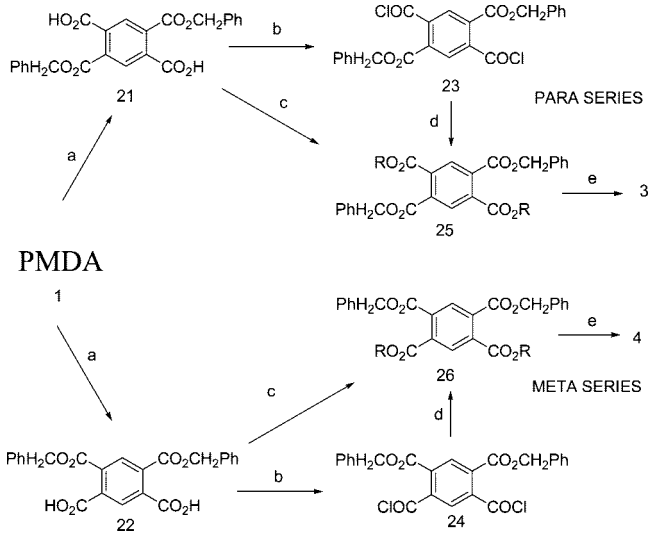
Mechanism of the Minor Ester Exchange Observed with Orthoformate Esters and Pyromellitates. Minor ester exchange upon pre-existent ester functionality was detected by GC/MS in several of the systems (Scheme 2). The maximum extent of ester exchange observed was in the preparation of meta diethyl dimethyl pyromellitate (**7a** = **7b**). Both possible combinations of reagents, viz., meta dimethyl pyromellitate (**4a**) with triethyl orthoformate or meta diethyl pyromellitate (**4b**) with trimethyl orthoformate, gave product (**7a**, **7b** respectively) of 95−96% purity. The sole byproduct observed in each case (**11** or **13**, respectively) bore three alkyl groups derived from the orthoformate, and one from the original diester. No homogeneous tetraesters (**5**) corresponding to the orthoformate were observed in any of the illustrated systems.

It was further noted that *no* byproduct was observed in the esterification of ortho diethyl pyromellitate anhydride (**14**, see below, Scheme 3) with trimethyl orthoformate and methanol. Furthermore, the triethyl methyl (**11**) and ethyl trimethyl (**13**) esters, prepared from the appropriate triester (**10b** or **10a**, respectively), each contained a single byproduct (1% or 4%, respectively). This was identified as a diethyl dimethyl ester, the GC/MS fragmentation pattern of which was characteristic specifically of the ortho isomer **12.** As can be seen from the following discussion, the fragmentation pattern of **12** is easily distinguishable from the fragmentation patterns of the para (**6a**) or meta (**7a** = **7b**) isomers.

Pyromellitate tetraesters containing only methyl and/or ethyl substituents have weak molecular ions, usually 2% or less of the base peak in relative intensity. The most important diagnostic fragmentation modes involve losing 31 Da if methoxy is present, 45 Da if ethoxy is present, 59 Da (31 + 28) if both methoxy and ethoxy are present (and strong if methoxy and ethoxy are adjacent; much weaker if they are not), and 73 Da (45 + 28) if at least two ethoxy groups are present, and providing maximum

(23) Toker, S. U.S. Pat. 3,326,851 (CA 67: 64908t).

SCHEME 5. Benzyl-ester Assisted Synthesis of Para and Meta Pyromellitate Diesters[a]



[a] Numbering for compounds **25** and **26**: "a"-Series: R = Me; "b"-Series: R = Et. Reagents and conditions: (a) $PhCH_2OH$, Et_3N, CH_2Cl_2, rt to reflux; (b) $(-COCl)_2$, CH_2Cl_2, catalytic $HCONMe_2$, reflux; (c) $HC(OR)_3$, reflux; (d) ROH, Et_3N, CH_2Cl_2, rt; (e) H_2, Pd−C, THF, 1 atm, rt.

intensity if two ethoxy groups are adjacent. M-73 Da is thus the base peak for ortho diethyl dimethyl pyromellitate (**12**) (at 265 Da), for triethyl methyl pyromellitate (**11**) (at 279 Da), and for tetraethyl pyromellitate (**5b**) (at 293 Da). M-45 Da becomes the base peak if all ethoxy groups present are nonadjacent and thus provides the base peak for the meta (**7a,7b**) or para (**6a**) diethyl dimethyl pyromellitates (at 293 Da) and for ethyl trimethyl pyromellitate (**13**) (at 279 Da). M-59 Da (at 279 Da) is strong (about 50% relative intensity) for **7a,b** or **6a** but weak (9% relative intensity) for **12**. Further differences are laid out in tabular form in Supporting Information (Table 9).

The above observations are consistent with the following conclusions: (1) Adjacent (vicinal) diester moieties do not exchange with alcohol or orthoformate under our conditions. (Evidence: the ortho diester system leading to **12** produced no detectable exchanged byproducts). (2) Therefore, ester exchange is associated with the hemiphthalate moieties of a pyromellitate and behaves as if it were to occur via reversible thermal formation of the anhydride from such moieties, as will be further discussed for Scheme 3, below. (Evidence: observation of specifically the ortho diethyl dimethyl ester **12** as byproduct from the esterification of triesters **10a** or **10b**). However, the actual mechanism could involve an intermediate condensation product between the carboxylic acid group and the orthoformate ester, rather than an anhydride group as such. (3) Pyromellitate diesters do not appear to undergo ester-exchange reactions enroute to the triester intermediates in the per-esterification (Evidence: homogeneous tetraesters **5** were not observed among the products of Scheme 2). (4) Therefore, the ester exchange process operates primarily at the pyromellitate triester stage. (5) The exchange process introduces one extra esterifying substituent derived from the orthoformate reagent. The lack of ester exchange among pre-existing vicinal diesters implies that these cannot be converted to orthoesters of pyromellitates by orthoformate esters under our conditions. Also, the observed transesterification should be seen as being idiosyncratic to situations where cyclic anhydrides (or similar intermediates) can form reversibly from the substrate, rather than as a general property of orthoformate esterification.

The choice of orthoformate esters as a reagent for esterifying *compatible* carboxylic acids was reported in 1965,[22a] but the method appears to have received surprisingly little use since. The yields originally reported only ranged from 54% to 94%. Such yields deceptively appear to be mediocre. However, the original work tended to include neither an excess of orthoformate nor an adequate reaction time. By ensuring an excess of orthoformate reagent and adequate time, esterification can be driven to completion. This has already been demonstrated with substrates such as nicotinic acids.[22b] Orthoformate esterification compares favorably to a recently reported[22c] procedure involving the addition of thionyl chloride to an alcoholic solution of a phthalic acid or anhydride which proceeded in yields of 61% to 90%.

Pyromellitate Triesters: Precursors to Ortho Diesters. While para (**3**) and meta (**4**) diesters of pyromellitic acid are readily available by the direct reaction of PMDA (**1**) with alcohols, the ortho diester (e.g., **15**) requires esterification of a pair of *adjacent* carboxyl groups and therefore has to be prepared indirectly, when PMDA is the ultimate precursor. One way of ensuring adjacent esterification is to start with the now readily obtained tetraesters (e.g., **5b**) and attempt a partial saponification to obtain the desired result. Although reaction with 2 equiv of alkali led to hopeless mixtures, with 1 equiv of NaOH, useful quantities of triethyl pyromellitate (**10b**) could be readily obtained, albeit in an impure form (Scheme 3).

The hemiphthalate side of a pyromellitate triester (**10**) shares with all phthalic acid half-esters a significant interaction between the adjacent carboxyl groups: the ability to form a cyclic anhydride upon pyrolysis. The reaction between phthalic anhydrides and alcohols to give phthalate monoesters (hemiphthalates) is well-known to be thermally reversible. This reversibility was invoked above as a possible explanation of the observed transesterification byproducts and can be exploited. The diester side of a pyromellitate triester (**10**) may have no ready path for decomposition open to it, if the esterifying alkyl groups themselves are thermally stable. [The remarkable thermal stability of certain pyromellitate tetraesters was considered noteworthy enough to be mentioned in Beilstein.[3]] Upon heating (to above 180 °C), triethyl pyromellitate (**10b**) proceeded to expel ethanol and gave ortho diethyl pyromellitate anhydride (**14**). In the impure system at hand, any ortho diethyl pyromellitate (**15**) present also would be expected to decompose to give **14**. Meanwhile, all of the other pyromellitic acids possibly present [meta (**4b**) or para (**3b**) diesters, the monoester (**9b**), or the free parent tetracarboxylic acid] should decompose to regenerate PMDA (**1**) itself. Thus in principle, the potentially complex saponification mixture converged as it decomposed upon distillation to give only two product anhydrides, **1** and **14**. The resulting PMDA (**1**) was readily removed since it was poorly soluble in CH_2Cl_2. Ortho diethyl pyromellitate anhydride (**14**) was then readily purified by crystallization.

In practice, the reaction was complicated by the formation of one additional product, the corresponding tetraester (**5b**), by disproportionation. The tetraester was observed to form, even when high-purity triester samples were pyrolyzed, and so was not an artifact. Evidently, the evolved alcohols can be intercepted in part, before distilling from the mixture, by high molecular

weight *acyclic* mixed anhydrides[24] of pyromellitate triesters. That such mixed anhydrides do not persist in the reaction mixture is evidenced by the negligible residue remaining after Kugelrohr distillation. Tetraester **5b** remained in the mother liquors of the crystallization of **14**.

The purified anhydride (**14**) readily reacted with ethanol to regenerate pure triethyl pyromellitate (**10b**). Anhydride-formation was thus an effective strategy for the purification of the triester (**10b**). Alternatively, aqueous hydrolysis (in acetic acid) of **14** led to the desired ortho diethyl pyromellitate (**15**) free acid, isolated as the monohydrate. Methanol and trimethyl orthoformate converted **14** to ortho diethyl dimethyl pyromellitate (**12**) (Scheme 3), which was found to be free of transesterified byproducts, as noted above.

Characterization of the anhydrides we report was done by NMR and not IR spectroscopy. The presence of the anhydride ring makes itself obvious in ^{13}C NMR spectra of pyromellitate derivatives, as can be observed by comparing the spectra of **14** and **15**. Ortho diethyl pyromellitate **15** has its carboxylic acid carbonyl groups at δ 171 and its ester groups at δ 165.4, typical of pyromellitate esters. Anhydride **14** has ester carbonyls at the normal δ 165.0, but the anhydride carbonyls occur at δ 161.1. The benzene ring also reflects major differences. Whereas the unstrained diacid **15** has carbonyl-substituted carbons at δ 133 and 135 and the protonated carbons at the normal position at δ 129.7, for the anhydride **14**, these carbon resonances are significantly shifted, occurring at δ 132.9 and significantly downfield at δ 139.5 for the carbonyl-substituted carbons and significantly shifted upfield at δ 126.2 for the protonated carbons. Similar features are also observed in the other anhydrides we report.

This strategic approach to ortho disubstituted pyromellitates would appear to be quite general, subject only to limitation by the possible thermal instability of the chosen esterifying group. This substitution pattern may well have application in the synthesis of ester-substituted phthalocyanines.[25,26]

Trimethyl pyromellitate has been reported[27] as the result of a selective saponification of tetramethyl pyromellitate (**6a**) with 1,1-dimethylhydrazine. This reagent effects S_N2 attack on the ester methyl group to give a 1,1,1-trimethylhydrazinium salt and may well be ineffective for more hindered esters. A bis tributylstannyl derivative of ortho substitution pattern has been reported[28] for pyromellitic acid.

Benzyl Esters of Pyromellitic Acid and Application to the Regioselective Synthesis of Other Esters. Benzyl Ester Routes to Triesters. Because of the awkward solubility properties associated with higher molecular weight materials, other pyromellitate tetraesters would not be expected to saponify as smoothly as the ethyl ester (**5b**). Thus an alternative approach to pyromellitate triesters was devised employing benzyl esters, which can be selectively cleaved by catalytic hydrogenolysis over palladium (Scheme 4). This relied on the prior differentiation of one of the carboxylate groups as a benzyl ester, to be followed by esterifying the remaining carboxylate groups with the desired alcohol, using either orthoformate or acid chloride chemistry.

A benzyl trialkyl pyromellitate (**20**) could be generated in a (nearly) one-pot sequence from PMDA (**1**) using triethylamine/dichloromethane, by adding 1 equiv of benzyl alcohol initially, to be followed after an appropriate delay by the second alcohol. After an acid workup to remove triethylamine, esterification was completed on the crude product using the corresponding orthoformate ester. Kugelrohr distillation of **20** served to remove some of the ester byproducts. Inasmuch as the initial reaction of PMDA with benzyl alcohol was not entirely selective, dibenzyl dialkyl (e.g., **25** and **26**, Scheme 5) and tetraalkyl pyromellitates (**5**) were present as well. Although impure triester product (**10**) resulted after hydrogenolysis, it could be handled similarly to the crude triester resulting from the saponification method. Left unexplored was the possible approach of transesterifying tetraethyl pyromellitate (**5b**) with 1 equiv of benzyl alcohol to generate **20** and then separating the resulting mixture by Kugelrohr distillation.

Much purer benzyl trialkyl pyromellitate (**20**) resulted from the use of purified monobenzyl pyromellitate (**17**) in the synthesis (Scheme 4). The product (in $Et_3N-CH_2Cl_2$) from the reaction of PMDA with 1 equiv of benzyl alcohol was shaken with excess dilute HCl, and the organic phase was isolated promptly. Under these conditions, monobenzyl pyromellitate anhydride (**16**) persisted and could be induced to crystallize. It proved to crystallize especially well as a 1:1 adduct with acetic acid, a feature of pyromellitate chemistry shared at least with the mono-*l*-menthyl ester analog as well.[5] The optimum workup would then include the addition of acetic anhydride and acetic acid to the CH_2Cl_2 phase after the HCl treatment. The resulting crystalline monobenzyl pyromellitate anhydride (**16**) hydrolyzed smoothly in aqueous acetic acid to monobenzyl pyromellitate (**17**). When **17** was refluxed with trimethyl or triethyl orthoformate, the desired benzyl trialkyl pyromellitates (**20a** or **20b**) were obtained in near-quantitative yield, and the products obtained contained only minor (<2%) quantities of the corresponding tetraalkyl esters **5a** or **5b**. Hydrogenolysis of either **20a** or **20b** led to the appropriate trialkyl pyromellitate (**10a** or **10b**), from which in turn were also prepared the mixed ethyl trimethyl (**13**) and triethyl methyl (**11**) derivatives, in addition to the anhydrides (**14** and **14a,** "Et" = Me).

Since the orthoformate esters are impractical for most desired substituents, a more general alternative approach to benzyl trialkyl pyromellitates was devised involving the use of acid-chloride chemistry (Scheme 4). Monobenzyl pyromellitate (**17**) reacted with excess oxalyl chloride in CH_2Cl_2 containing catalytic *N*,*N*-dimethylformamide to give (as evidenced by ^{13}C NMR) two principal products. Surprisingly, the originally expected monobenzyl pyromellitate anhydride acid chloride (**18**) was only a minor (<20%) component.[29] The principal product (ca. 80%) proved to be monobenzyl pyromellitate triacid chloride (**19**). This actually simplified matters for the case at hand: the crude triacid chloride (**19**) as obtained above was reacted with an excess of an alcohol and Et_3N in CH_2Cl_2 to

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(27) Kasina, S.; Nematollahi, J. *Tetrahedron Lett.* **1978**, 1403–1406.

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(29) (a) The current relative inaccessibility of pyromellitate anhydride acid chlorides such as **15** stymied a facile synthesis of triesters, which would have entailed their reaction with 2 equiv of an alcohol. Pyromellitic anhydride diacid chloride has been reported[29b] and could presumably be used similarly with 3 equiv of an alcohol. (b) Baker, W. R.; Rosenberg, S. H.; Fung, K. L. A.; Rockway, T. W.; Fakhoury, S. A.; Garvey, D. S.; Donner, B. G.; O'Connor, S. J.; Prasad, R. N.; Shen, W.; Stout, D. M.; Sullivan, G.M. WO 9634851 A1 961107 (CA 126:59751)

give the benzyl trialkyl pyromellitate (**20**). This could be readily isolated in pure form by chromatography. Since this chemistry was all performed with chiral derivatives (*l*-menthol), the experimental details are presented in the following paper.[5]

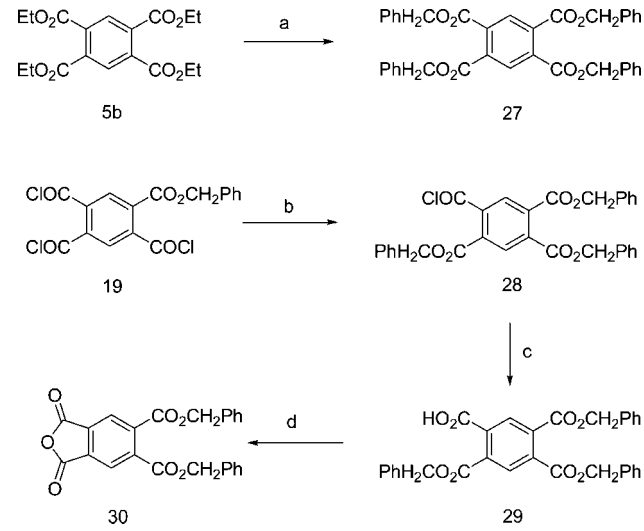
Benzyl Ester Routes to Diesters. Benzyl esters could be similarly employed to prepare specific dialkyl pyromellitates (Scheme 5). The reaction of PMDA (**1**) with 2 equiv of benzyl alcohol in Et_3N-CH_2Cl_2, followed by the usual workup, led to the meta- para mixture of dibenzyl esters[30] (**21**,**22**). This mixture could be separated by sequential crystallization from acetic acid - water. The benzyl ester system was therefore much more easily separable (by crystallization) than the mixtures derived from the direct reaction of PMDA with the lower alcohols (methanol, ethanol, etc.). Thus, pure samples of the para or meta dimethyl or diethyl pyromellitates (**3a**,**b**; **4a**,**b**) were obtained by reaction of the appropriate pure dibenzyl ester isomer with the desired orthoformate ester, followed by hydrogenolytic cleavage of the benzyl groups (Scheme 5). Since the dibenzyl dialkyl pyromellitates (**25**, **26**) that were prepared were crystalline substances, any traces of transesterification products were lost in the mother liquors of the crystallization procedure.

Alternatively, reaction of either dibenzyl ester isomer (**21**, **22**) with oxalyl chloride in CH_2Cl_2 with DMF catalysis afforded the crystalline para (**23**) or meta (**24**) dibenzyl pyromellitate diacid chlorides. To avoid solubility losses, for maximal yield in use, the acid chlorides would be used without purification and reacted directly with alcohols and Et_3N in CH_2Cl_2. Again, the examples of this entailed the use of chiral alcohols and so the experimental procedures for the alcoholysis are deferred until the following paper.[5] The use of a specific dibenzyl ester would allow the minimal diversion of *valuable* alcoholic substrates into the formation of the "wrong" isomer, an unavoidable feature of the direct reaction of an alcohol with PMDA. Oxalyl chloride was used for the acid chloride synthesis rather than thionyl chloride so as to avoid any chance of sulfur-containing impurities interfering with subsequent hydrogenolyses.

Since the availability of ortho dibenzyl pyromellitate anhydride (**30**) would similarly ease the path to a wide range of ortho pyromellitate diesters, an approach to that substance was investigated (Scheme 6).

Tetrabenzyl pyromellitate[31] (**27**) was prepared by a method also used for terpene-derived pyromellitate tetraesters,[5] viz., the base-catalyzed (NaH) transesterification of tetraethyl pyromellitate (**5b**) in boiling xylene with a moderate excess of benzyl alcohol (Scheme 6). The resulting tetrabenzyl pyromellitate (**27**) proved to be far too insoluble in any of the desired solvents to be of practical use. Therefore, instead of attempting the approach to **30** by degradation of a tetraester, the alternative of synthesis by assembly was examined. The above-noted reluctance of monobenzyl pyromellitate anhydride acid chloride (**18**) to form from monobenzyl pyromellitate (**17**) under our chosen conditions ruled out a smooth synthesis of the tribenzyl ester (**29**) involving the reaction of **17** with 2 equiv of benzyl alcohol. Instead, monobenzyl pyromellitate anhydride (**16**) was converted to crude monobenzyl pyromellitate triacid chloride (**19**), and the latter was reacted with about 2 equiv of benzyl alcohol. Crude tribenzyl pyromellitate (**29**) arose thereby, contaminated by the poorly soluble tetraester (**27**) (Scheme 6).

SCHEME 6. Synthesis of Ortho Dibenzyl Pyromellitate Anhydride (26)[a]



[a] Reagents and conditions: (a) $PhCH_2OH$, catalytic NaH, xylene, reflux; (b) 2 $PhCH_2OH$, Et_3N, CH_2Cl_2, rt to reflux; (c) H_2O, HOAc, brief reflux; (d) pyrolysis in vacuo; distillation.

Triester **29** decomposed in the usual manner upon Kugelrohr distillation to give benzyl alcohol and the anticipated ortho dibenzyl pyromellitate anhydride (**30**), which could be distilled away from any contaminating **27**. The experimental details are less polished than for the remaining work and are therefore confined to the Supporting Information. Enough was accomplished to demonstrate that the approach was viable; in particular, it was established that it was possible for the ortho-paired benzyl esters to survive the pyrolysis conditions, given a suitably high vacuum.

General Synthesis of Pyromellitate Esters from PMDA. In principle, the chemistry described herein could allow up to four different esterifying groups to be appended to the pyromellitate system. The overall strategy involves sequential esterification of monobenzyl pyromellitate anhydride (**16**) by two different alcohols to generate a tetraester meta/para mixture. Removal of the benzyl group by hydrogenolysis, and pyrolytic anhydride formation should lead convergingly from the mixture to an ortho diester anhydride with two *different* esterifying groups. Further alcoholysis will then provide a binary mixture in need of separation and characterization, before further esterification.

Experimental Section

General Procedures. Reagents were used as received, unless otherwise noted. Methanol was distilled from magnesium methoxide, benzyl alcohol was distilled (1 atm) from K_2CO_3, and triethylamine was distilled twice, the first time being from phthalic anhydride (this serves to remove lower amines that result from autoxidation during storage). Mass spectra were obtained under GC/MS conditions, unless otherwise noted. The Kugelrohr used was an older version heated by variable transformer, without thermostatic temperature control; external temperatures varied over a wide range during distillations. Where xylene is specified as solvent, any isomer or mixture will do. Melting points were determined (in air) preliminarily in capillary tubes and then refined using a hot stage with polarizing microscope and slow heating rates, to better observe phase transitions.

Tetraethyl Benzene-1,2,4,5-tetracarboxylate (Tetraethyl Pyromellitate) (5b). PMDA (**1**) (219.3 g, 1.005 mol), triethyl or-

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(32) Campbell, W. P.; Soffer, M. D. *J. Am. Chem. Soc.* **1942**, *64*, 417–425.

thoformate (505 mL, 3.036 mol), and EtOH (120 mL, 100%, 2.056 mol) were refluxed (Vigreux column with "solvent" still head) for 4.5 h. Low-boilers were removed from the trap periodically and discarded if boiling below 80 °C or recycled if boiling above. Heating was terminated when the vapor temperature atop the Vigreux column exceeded and remained above 146 °C with total reflux. (Reaction completion was confirmed by TLC.) The excess triethyl orthoformate was removed [rotary evaporator/boiling water bath, followed by Kugelrohr distillation: bp ≤142 °C (external)/1 Torr]. The product was recovered by Kugelrohr distillation into a fresh set of receiver bulbs, bp 185−227 °C (external)/0.5 Torr. The distillate solidified in the receiver. It was remelted (heat gun) to facilitate bottling. Yield: 365.5 g (0.998 mol, 99.2%). Mp (of the solidified distillate) 53.3−55.0 °C (lit.[3] 53 °C); ^{1}H NMR ($CDCl_3$) δ 1.38 (12H, t, J = 7.2 Hz), 4.39 (8H, q, J = 7.2 Hz), 8.04 (2H, s); ^{13}C NMR ($CDCl_3$ at 77.1) δ 166.0 (4C), 134.4 (4C), 129.5 (2C), 62.2 (4C), 14.1 (4C); MS, *m*/*z* (relative intensity) 366 [M^+] (2), 322 (2), 321 (43), 294 (11), 293 (100), 276 (2), 265 (12), 248 (3), 247 (5), 237 (4), 221 (14), 219 (15), 193 (18), 176 (5), 165 (5), 149 (2), 148 (22), 147 (20), 120 (5), 119 (6), 109 (4), 103 (3), 102 (2), 92 (3), 91 (9), 81 (5), 75 (4), 73 (4), 64 (3), 63 (3), 53 (3), 45 (6), 44 (6), 43 (3).

Diethyl 1,3-Dioxo-1,3-dihydroisobenzofuran-5,6-dicarboxylate (Ortho Diethyl Pyromellitate Anhydride) (14). Method A. A magnetically stirred solution of tetraethyl pyromellitate (**5b**) (73.3 g, 0.20 mol) and thymolphthalein (ca. 200 mg) in EtOH (400.9 g, 100%) was treated, at room temperature, slowly dropwise with a solution of NaOH (7.25 g, 0.18 mol) in H_2O (100 mL). The NaOH solution was rinsed in with EtOH (24.2 g, 100%). The mixture was stirred until the indicator faded and then let stand overnight. The solvent was removed (rotary evaporator), and the residue was partitioned between H_2O (500 mL) and Et_2O (250 mL, then 200 mL) [From this, 20.74 g (28.3%) of tetraethyl pyromellitate (**5b**) was recovered.] The aqueous phase was acidified with concentrated HCl (21.4 mL) and extracted with Et_2O (2 × 200 mL). The solvent was removed (rotary evaporator), and the resulting residue (crude **10b**, 48.1 g) was distilled (Kugelrohr). Triethyl pyromellitate (**10b**) decomposed above ca. 180 °C. The resulting anhydride (**14**) distilled over at ca. 265−270 °C (external)/5 Torr (est), solidifying promptly in the receiver. The yield of crude distillate was 42.4 g. The product (40.4 g) was stirred with CH_2Cl_2 (100 mL) until the lumps disintegrated. Byproduct PMDA (**1**) (1.6 g) was filtered off and rinsed with CH_2Cl_2 (40 mL). *n*-Hexane (100 mL) was added to the filtrates, which were then concentrated carefully on a rotary evaporator at 50 °C until colorless needles separated in quantity. Further *n*-hexane (100 mL) was added, and the evaporation continued until a thick slurry resulted. The solids were filtered off, rinsed with *n*-hexane, and then dried in a desiccator over KOH. Yield: 31.8 g (0.109 mol, 57.1% or 79.6% based on unrecovered **5b**). Mp 99−104 °C, with recrystallization at 103.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.42 (6H, t, J = 7.2 Hz), 4.46 (4H, q, J = 7.2 Hz), 8.33 (2H, s); ^{13}C NMR ($CDCl_3$ at 77.1) δ 165.0, 161.1, 139.5, 132.9, 126.2, 63.0, 14.0 (2 C all peaks); MS (direct probe) *m*/*z* (relative intensity) 293 (1), 292 [M^+](2), 265 (2), 248 (5), 247 (32), 237 (1), 221 (2), 220 (9), 219 (100), 192 (3), 191 (4), 176 (3), 175 (5), 174 (18), 148 (10), 147 (54), 120 (4), 119 (11), 103 (8), 102 (36), 91 (30), 76 (2), 75 (14), 74 (37), 73 (14), 65 (3), 63 (9), 62 (6), 61 (2), 53 (4), 51 (4), 50 (3), 47 (6), 45 (14), 44 (6), 43 (5), 39 (1). Anal. Calcd for $C_{14}H_{12}O_7$: C, 57.54; H, 4.14. Found: C, 57.46; H, 4.01. **Method B.** A Kugelrohr distillation of triethyl pyromellitate (**10b**) (3.39 g, 10.02 mmol), derived from the hydrogenolysis of benzyl triethyl pyromellitate (**20b**) (see below), gave 2.81 g (96.0%) of crude **14** [bp 177−202 °C (external)/0.75−1 Torr].

4,5-Bis(ethoxycarbonyl)phthalic Acid Monohydrate (Ortho Diethyl Pyromellitate Monohydrate) (15). Ortho diethyl pyromellitate anhydride (**14**, from Method A) (5.85 g, 0.02 mol) was dissolved in glacial HOAc (10.0 mL). H_2O (10.0 mL) was added slowly until permanent opalescence. On heating (water bath) it became possible to add the remaining H_2O without causing precipitation. After 30 min at 100 °C, the solvent was removed in vacuo and chased with H_2O. The residue crystallized on standing. It was triturated with minimal H_2O. The solids were filtered off, washed with minimal H_2O, and dried. Yield: 6.18 g (0.0188 mol, 94%). Mp 110.0−115.5 °C, with dehydration and partial recrystallization; remelted 155.5−161.1 °C; ^{1}H NMR ($CDCl_3$) δ 1.40 (6H, t, J = 7 Hz), 4.43 (4H, q, J = 7 Hz), 7.55 (4H, br s), 8.19 (2H, s); ^{13}C NMR ($CDCl_3$ at 76.9) δ 171.3, 165.4, 135.0, 133.0, 129.7, 62.4, 14.0 (2C each peak). Anal. Calcd for $C_{14}H_{14}O_8$: C, 54.20; H, 4.55. Calcd. for $C_{14}H_{14}O_8.H_2O$: C, 51.22; H, 4.91. Found: C, 50.85; H, 4.78

2,4,5-Tris(ethoxycarbonyl)benzoic Acid (Triethyl Pyromellitate) (10b). Method A. A solution of ortho diethyl pyromellitate anhydride (**14**, from Method A) (5.85 g, 0.02 mol) in absolute EtOH (50 mL) was refluxed for 10 min. The solvent was removed in vacuo, and the residual viscous oil gradually crystallized. Yield: 6.78 g (0.02 mol, quantitative). A sample (5.59 g) was recrystallized from aqueous acetic acid, with repeated warming and cooling to overcome a tendency to oil. Recovery: 4.12 g. Mp 73.4−76.3 °C; ^{1}H NMR ($CDCl_3$) δ 1.39 (3H, t, J = 7 Hz), 1.40 (6H, t, J = 7 Hz), 4.420 and 4.422 (6H, overlapping q, J = 7 Hz), 8.03 (H, s), 8.25 (H, s), 10.97 (H, br s); ^{13}C NMR ($CDCl_3$ at 76.9) δ 170.4, 165.96, 165.69, 165.41, 135.33, 135.25, 133.8, 131.9, 130.1, 129.1, 62.42, 62.26 (2C), 14.03 (2C), 13.87 (each peak 1C unless otherwise noted). Anal. Calcd for $C_{16}H_{18}O_8$: C, 56.80; H, 5.36. Found: C, 56.62; H, 5.67. **Method B.** A solution of benzyl triethyl pyromellitate (**20b**) (21.52 g, 50.23 mmol) in THF (153 mL, freshly redistilled through a rotary evaporator to remove preservatives or other nonvolatiles) with 10% Pd/C (0.74 g), was stirred under H_2 (1 atm, ambient temperature) until gas uptake ceased. The catalyst was removed by filtration, and the filtrates were evaporated to dryness on the rotary evaporator. The resulting residual oil crystallized over several days after seeding. Traces of remaining toluene were permitted to evaporate as the solidification proceeded. Yield: quantitative (50.2 mmol, 17 g). Mp 72.0−76.0 °C. The material was identical (^{1}H and ^{13}C NMR) with material prepared previously by Method A.

1,2-Diethyl 4,5-Dimethyl Benzene-1,2,4,5-tetracarboxylate (Ortho Diethyl Dimethyl Pyromellitate) (12). From ortho diethyl pyromellitate anhydride (**14**) (5.85 g, 0.02 mol), MeOH (10 mL), and trimethyl orthoformate (30.7 mL) after reflux (3 h) and distillation (Kugelrohr) at 218−224 °C (external)/0.34 Torr. The product was isolated as an oil, in quantitative yield (6.77 g, 0.02 mol). ^{1}H NMR ($CDCl_3$) δ 1.38 (6H, t, J = 7.1 Hz), 3.94 (6H, s), 4.41 (4H, q, J = 7.1 Hz), 8.09 (2H, s); ^{13}C NMR ($CDCl_3$ at 77.3) δ 166.4, 165.9, 134.6, 134.1, 129.6, 62.3, 53.1, 14.1 (2C all peaks); GC/MS *m*/*z* (relative. intensity) 338 [M^+] (2), 307 (25), 293 (30), 279 (9), 266 (13), 265 (100), 251 (6), 237 (5), 234 (5), 233 (20), 221 (4), 220 (5), 207 (37), 179 (5), 177 (21), 163 (24), 161 (30), 148 (25), 136 (6), 133 (7), 119 (27), 104 (7), 103 (10), 102 (12), 91 (19), 77 (7), 76 (14), 75 (45), 65 (16), 59 (18). Anal. Calcd for $C_{16}H_{18}O_8$: C, 56.80; H, 5.36. Found: C, 56.91; H, 5.26.

5-(Benzyloxycarbonyl)-1,2,4-benzenetricarboxylic Acid (Benzyl Pyromellitate) (17). A stirred suspension of PMDA (**1**)(234.2 g, 1.074 mol) in a solution of benzyl alcohol (110.2 g, 1.019 mol) in CH_2Cl_2 (775 mL) was treated, over a 2 min period, with a steady stream of Et_3N (111.5 g, 154 mL, 1.102 mol). The PMDA dissolved during this addition, and the mixture boiled spontaneously. After 1 h, the solution was filtered, and the apparatus and filter were rinsed with CH_2Cl_2 (225 mL). The CH_2Cl_2 phase was shaken with concentrated HCl (100 mL) in H_2O (530 mL) and quickly isolated from the aqueous phase, before product could crystallize. The organic phase soon became thick with solids. These were filtered off and rinsed with CH_2Cl_2. A second crop was obtained after concentrating the filtrates to 25% of the original volume. (See the preparation of *l*-menthyl pyromellitate in the following paper[5] for a modification, i.e., workup with acetic acid/acetic anhydride, that should improve the yield here as well.)

The light tan monobenzyl pyromellitate anhydride (**16**) (moist filter cake) was slurried in glacial HOAc (250 mL) and then rotary evaporated at 100 °C to remove CH_2Cl_2. Further HOAc (250 mL) was added, followed by H_2O (100 mL). The slurry was heated (water bath, 100 °C), and the solids dissolved completely. After a few minutes, product began to crystallize out. About 400 mL of the solvent was removed in vacuo (rotary evaporator). Water (100 mL) was added to the remainder, and the product was isolated by filtration. The solids were washed with 50% (v/v) aqueous acetic acid and H_2O, and then allowed to dry in air. Yield: 159.6 g, (45.5%). A similar hydrolysis of the second crop anhydride (**16**) afforded an additional 37.9 g (10.8%). Total: 197.5 g, (0.574 mol, 56.3%). Mp 210.0−222.0 °C (dec); ^{1}H NMR (CD_3OD) δ 4.95 (CO_2H, H_2O), 5.35 (2H, s), 7.32−7.45 (5H, m), 7.98 (H, s), 8.12 (H, s); ^{13}C NMR (CD_3OD at 49.0) δ 169.37, 169.33, 168.7, 168.1, 136.63, 136.55, 136.14, 135.98, 135.42, 130.7, 130.0, 129.55 (2C), 129.43 (2C), 129.40, 69.1 (1C each peak unless otherwise noted). Anal. Calcd for $C_{17}H_{12}O_8$: C, 59.31; H, 3.51. Found: C, 59.09; H, 3.45.

6-(Benzyloxycarbonyl)-1,3-dioxo-1,3-dihydroisobenzofuran-5-carboxylic Acid, 1:1 Solvate with Acetic Acid. (Monobenzyl Pyromellitate Anhydride, 1:1 Acetic Acid Adduct) (16). A suspension of monobenzyl pyromellitate (**17**) (34.6 g, 0.101 mol) in glacial HOAc (100 mL) was heated to boiling. Acetic anhydride (20 mL) was added. Within minutes, the solids dissolved. After 1 min of further reflux, the hot solution was decanted from the boiling chips. The cooling solution deposited coarse transparent chunky needles. These were filtered off, rinsed with EtOAc, EtOAc/hexane, and finally hexane, and dried over KOH. Yield: 33.71 g (0.0873 mol, 86.8%). Mp 180.5−184.5 °C (dec), after slow heating to drive off acetic acid; ^{1}H NMR (acetone-d_6) δ 1.97 (3 H, s, $\mathbf{CH_3}CO_2H$), 5.39 (2 H, s, Ph$\mathbf{CH_2}$O), 7.34−7.42 (3 H, m, Ph), 7.46−7.50 (2 H, m, Ph), 8.32 (H, d, J = 0.79 Hz), 8.40 (H, d, J = 0.78 Hz). (Spectrum not observed beyond δ 8.9.); ^{13}C NMR (acetone-d_6 at 29.8 and 207.0) δ 172.8, 166.36, 166.23, 162.4, (4 peaks for 5 C=O, it was unclear from the spectrum appearance as to which peak was degenerate, although logically the degenerate peak should be that for the anhydride carbonyls at 162; significant shifts were noted here as compared to the *l*-menthyl analog in $CDCl_3$ (see following paper); the compound was hydrolyzed in DMSO-d_6) 140.4, 139.6, 136.1, 134.53, 134.24, 129.31 (2 C), 129.20 (3 C), 126.7, 126.2, 68.8, 20.5 (1C each peak unless otherwise noted). Anal. Calcd for $C_{17}H_{10}O_7$: C, 62.58; H, 3.09. Calcd for $C_{17}H_{10}O_7.C_2H_4O_2$: C, 59.07; H, 3.65. Found: C, 58.90; H, 3.55.

1-Benzyl 2,4,5-Triethyl Benzene-1,2,4,5-tetracarboxylate (Benzyl Triethyl Pyromellitate) (20b). A mixture of monobenzyl pyromellitate (**14**) (36.2 g, 0.105 mol), triethyl orthoformate (150 mL), and EtOH (50 mL, 100%) was refluxed, with periodic removal of low-boilers, until the vapor temperature reached 146 °C (5 h). Solids persisted for the first 2 h. When TLC (CH_2Cl_2−SiO_2) showed complete reaction, the excess reagent was removed (rotary evaporator, then Kugelrohr). The product was distilled [Kugelrohr, bp 222−237 °C (external)/0.72 to 0.95 Torr]. Yield: 43.6 g (0.102 mol, 96.4%) as a viscous oil. ^{1}H NMR ($CDCl_3$) δ 1.282 (3H, t, J = 7 Hz, Et), 1.367 (3H, t, J = 7 Hz, Et), 1.372 (3H, t, J = 7 Hz, Et), 4.254 (2H, q, J = 7 Hz, Et), 4.384 (2H, q, J = 7 Hz, Et), 4.389 (2H, q, J = 7 Hz, Et), 5.360 (2H, s, Ph$\mathbf{CH_2}$O), 7.314−7.437 (5H, m, Ph), 8.053 (H, s), 8.075 (H, s); ^{13}C NMR ($CDCl_3$ at 77.1) δ 165.95 (3C), 165.85, 134.99, 134.53 (2C), 134.43, 133.96, 129.62, 129.54, 128.65, 128.59 (2C), 128.55 (2C), 68.0, 62.2 (3C), 14.05 (2C), 13.98 (each peak 1C unless otherwise noted), Anal. Calcd for $C_{23}H_{24}O_8$: C, 64.48; H, 5.65. Found: C, 64.48; H, 5.76.

Dibenzyl Esters of Pyromellitic Acid (Para and Meta Dibenzyl Pyromellitate).[30] (A) 2,5-Bis(benzyloxycarbonyl)terephthalic Acid (Para Dibenzyl Pyromellitate) (21). PMDA (**1**) (109.5 g, 0.502 mol) and benzyl alcohol (111.0 g., 1.027 mol) (freshly distilled at 1 atm from K_2CO_3) were suspended in CH_2Cl_2 (560 mL). Redistilled triethylamine (105.5 g, 145 mL, 1.042 mol) was added to the magnetically stirred solution (2L Erlenmeyer) over 1 min. The mixture boiled vigorously and cleared as the amine was added. After standing overnight, the organic phase was shaken with concentrated HCl (101 mL)−H_2O (400 mL), and washed once with H_2O. The organic phase was stirred with Na_2SO_4 until clear and then decanted. Glacial acetic acid (300 mL) was added to the solution, which upon concentration in vacuo (rotary evaporator) deposited solids. The slurry was filtered, and the product was rinsed with HOAc. The filtrates, ca. 320 mL, were set aside, and the solids were rinsed further with 1:1 Et_2O−HOAc, and finally Et_2O. Yield: 73.6 g (0.169 mol, 33.8%), pure para isomer by NMR. A sample was recrystallized for analysis from EtOAc−THF. Mp 201.0−206.5 °C (dec); ^{1}H NMR (CD_3OD) δ 5.08 (H_2O), 5.33 (4 H, s), 7.274−7.438 (10 H, complex m), 8.06 (2 H, s); ^{13}C NMR (CD_3OD at 48.8) δ 168.53, 167.95, 136.67, 136.05, 135.90, 130.5, 129.56 (4 C), 129.47 (4 C), 129.41, 69.1 (all peaks 2C unless otherwise noted). Anal. Calcd for $C_{24}H_{18}O_8$: C, 66.36; H, 4.18. Found: C, 66.11; H 4.37.

(B) 4,6-Bis(benzyloxycarbonyl)isophthalic Acid (Meta Dibenzyl Pyromellitate) (22). The HOAc filtrates from the preceding experiment (320 mL) were diluted with H_2O (103 mL), without causing permanent opalescence. Overnight, the solution deposited masses of silky fibers. These were filtered off, washed thoroughly with 50% (v/v) aqueous acetic acid and then H_2O, and dried. Yield: 62.34 g (0.144 mol, 28.6%). This was found to be the pure meta isomer. The filtrates proved intractable and were discarded. Total yield of the pure isomers: 62.3%. A sample was recrystallized for analysis from ethyl acetate. Mp 183.5−187.5 °C; ^{1}H HNR (CD_3OD) δ 5.02 (H_2O, br s), 5.32 (4 H, s), 7.295−7.426 (10 H, complex m), 7.92 (H, s), 8.19 (H, s); ^{13}C NMR (CD_3OD at 49.0) δ 168.6, 168.0, 136.68, 136.40, 135.6, 131.1 (1C), 129.87 (1C), 129.58 (4C), 129.50 (4C), 129.44, 69.1 (all peaks 2C unless otherwise noted). Anal. Calcd for $C_{24}H_{18}O_8$: C, 66.36; H, 4.18. Found: C, 66.22; H, 4.05.

Dibenzyl 2,5-Bis(chlorocarbonyl)terephthalate (Para Dibenzyl Pyromellitate Diacid Chloride) (23). Para dibenzyl pyromellitate (**21**) (4.36 g, 0.01 mol), oxalyl chloride (3 mL, 4.37 g, 0.034 mol), *N*,*N*-dimethyl formamide (DMF) (3 drops), and dichloromethane (100 mL) were kept overnight at room temperature under moisture-exclusion conditions. The solution was filtered and then concentrated in vacuo (50 °C bath) until crystals appeared. *n*-Hexane (15 mL) was added to the crystallizing solution in portions. The dense colorless crystals were filtered, rinsed with 10% (v/v) CH_2Cl_2 in *n*-hexane (10 mL) and then *n*-hexane, and dried over KOH. Yield: 3.52 g (0.008 mol, 80.1%) Mp 129.5−133.5 °C (mostly 131.5−133.5 °C); ^{1}H NMR ($CDCl_3$) δ 5.39 (4H, s), 7.36−7.44 (10H, m), 8.14 (2H, s); ^{13}C NMR ($CDCl_3$ at 77.0) δ 166.6, 163.4, 139.7, 134.1, 132.0, 129.2, 128.97, 128.88 (4C), 128.76 (4C), 69.0 (2C each peak unless otherwise noted). Anal. Calcd for $C_{24}H_{16}Cl_2O_6$: C, 61.16; H, 3.42; Cl, 15.04. Found: C, 61.02; H, 3.44; Cl, 15.22.

Dibenzyl 4,6-Bis(chlorocarbonyl)isophthalate (Meta Dibenzyl Pyromellitate Diacid Chloride) (24). This was prepared from meta dibenzyl pyromellitate (**22**) (8.70 g, 20.03 mmol), oxalyl chloride (6 mL), and DMF (5 drops) in CH_2Cl_2 (100 mL). It crystallized in large chunks from dichloromethane−hexane. Minor tarry byproduct (Vilsmeier-reagent ?) which contaminated the early crops was eliminated by fractional crystallization. Yield: 3.93 g (0.00898 mol, 44.8%) in two crops. Mp 84−87 °C (mostly 85−86 °C); ^{1}H NMR ($CDCl_3$) δ 5.39 (4H, s), 7.35−7.43 (10H, m), 7.94 (H, d, J = 0.5 Hz), 8.37 (H, d, J = 0.5 Hz); ^{13}C NMR ($CDCl_3$ at 77.0) δ 166.5, 163.6, 139.8, 134.1, 132.0, 131.6 (1C), 128.91, 128.81 (4C), 128.74 (4C), 127.2 (1C), 68.9 (2C each peak unless otherwise noted). Anal. Calcd for $C_{24}H_{16}Cl_2O_6$: C, 61.16; H, 3.42; Cl, 15.40. Found: C, 61.11; H, 3.49; Cl, 14.79.

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Supporting Information Available: Experimental procedures and full characterization for compounds **2a**, **2b**, **3a**, **3b**, **4a**, **5a**, **6a**, **6b**, **7a**, **11**, **12**, **17a**, **22a**, **22b**, **23a**, **23b**, and **24**; experimental procedures and partial characterization for **8a**, **26**, and **27**; ^{13}C NMR chemical shift comparison tables, and ^{1}H NMR chemical shift comparison tables, and mass-spectral comparison of the methyl/ethyl pyromellitate mixed tetraester system. This material is available free of charge via the Internet at http://pubs.acs.org.

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