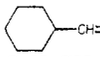
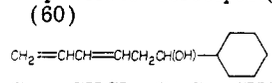
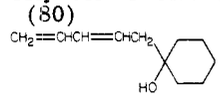
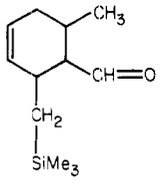
Table I. $TiCl_4$-Induced Pentadienylation of Aldehydes and Ketones by (2,4-Pentadienyl)trimethylsilane

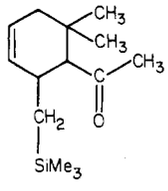
carbonyl compd	product alcohol (% yield)[a]
$CH_3CH_2CH{=}O$	$CH_2{=}CHCH{=}CHCH_2CH(OH)CH_2CH_3$ (79)
$(CH_3)_2CHCH{=}O$	$CH_2{=}CHCH{=}CHCH_2CH(OH)CH(CH_3)_2$ (80)
$(CH_3)_3CCH{=}O$	$CH_2{=}CHCH{=}CHCH_2CH(OH)C(CH_3)_3$ (60)
	 (58)
$C_6H_5CH{=}O$	$CH_2{=}CHCH{=}CHCH_2CH(OH)C_6H_5$ (51)
$(C_2H_5)_2C{=}O$	$CH_2{=}CHCH{=}CHCH_2C(OH)(C_2H_5)_2$ (55)
$(n\text{-}C_3H_7)_2C{=}O$	$CH_2{=}CHCH{=}CHCH_2C(OH)(C_3H_7\text{-}n)_2$ (80)
	 (64)

[a] In a few cases the 250-MHz ^1H NMR spectrum of the product was measured. It was found that the *E* isomer was the sole isomer present. All products were characterized by combustion analysis and by their IR and 60-MHz proton NMR spectra.

preparation of alcohols of the type $CH_2{=}CHCH{=}CHCH_2C(OH)RR'$ is in hand. The yields are fair to good and very likely can be improved when the reactions are carried out on a larger scale. The reaction conditions are quite mild, and the products which are obtained are isomerically pure. This reaction, however, is not readily applicable to the pentadienylation of α,β-unsaturated carbonyl compounds because of a competitive $TiCl_4$-induced Diels–Alder reaction.[6] Thus the reaction of crotonaldehyde with $Me_3SiCH_2CH{=}CHCH{=}CH_2$ in the presence of $TiCl_4$ under these conditions gave a 40% yield of II, while a similar reaction with mesityl oxide produced



II



III

a mixture of the Diels–Alder adduct (III, 24% yield) and the 1,4-addition product $[CH_2{=}CHCH{=}CHCH_2C(CH_3)_2CH_2C(O)CH_3]$ in 35% yield.

The mechanism of these pentadienylsilane addition reactions is not known as yet. Allylsilanes react with aldehydes and ketones in the presence of Lewis acids with allylic transposition, e.g., eq 3.[7] Experiments with appropriately substituted (2,4-pentadienyl)silanes will have to be carried out to determine whether or not the reactions proceed with pentadienyl transposition; i.e., is eq 4 applicable? Such studies are intended, as are further investigations of the chemical reactivity of $Me_3SiCH_2CH{=}CHCH{=}CH_2$ and related compounds.

$$Me_3SiCH_2CH{=}CHCH_3 + R_2C{=}O \xrightarrow{TiCl_4} \xrightarrow{H_2O} CH_2{=}CHC(CH_3)HC(OH)R_2 \quad (3)$$

$$Me_3SiCH_2CH{=}CHCH{=}CHCH_3 + R_2C{=}O \xrightarrow{TiCl_4} \xrightarrow{H_2O} R_2C(OH)C(CH_3)HCH{=}CHCH{=}CH_2 \quad (4)$$

(6) (a) T. Inukai and M. Kasai, *J. Org. Chem.*, **30**, 3567 (1965); (b) T. Inukai and M. Kojima, *ibid.*, **32**, 869 (1967).
(7) A. Hosomi and H. Sakurai, *Tetrahedron Lett.*, 1295 (1976).

Acknowledgment. The authors are grateful to the U.S. Air Force Office of Scientific Research (NC)-AFSC (Grant No. AF-AFOSR-79-0007) for support of this research. J.P. acknowledges with thanks a leave of absence from the University of Poitiers and the award of a NATO Postdoctoral Fellowship.

Registry No. II, 72952-63-7; III, 72952-64-8; propanal, 123-38-6; 2-methylpropanal, 78-84-2; 2,2-dimethylpropanal, 630-19-3; cyclohexanecarboxaldehyde, 2043-61-0; benzaldehyde, 100-52-7; 3-pentanone, 96-22-0; 4-heptanone, 123-19-3; cyclohexanone, 108-94-1; (*E*)-5,7-octadien-3-ol, 72952-65-9; (*E*)-2-methyl-5,7-octadien-3-ol, 72952-66-0; (*E*)-2,2-dimethyl-5,7-octadien-3-ol, 72952-67-1; (*E*)-1-cyclohexyl-3,5-hexadien-1-ol, 72952-68-2; (*E*)-1-phenyl-3,5-hexadien-1-ol, 72952-69-3; (*E*)-3-ethyl-5,7-octadien-3-ol, 72952-70-6; (*E*)-4-propyl-6,8-nonadien-4-ol, 72952-71-7; (*E*)-1-(2,4-pentadienyl)cyclohexanol, 72952-72-8; (*E*)-(2,4-pentadienyl)trimethylsilane, 72952-73-9; crotonaldehyde, 4170-30-3; mesityl oxide, 141-79-7; (*E*)-4,4-dimethyl-6,8-nonadien-2-one, 72952-74-0.

Dietmar Seyferth,* Jacques Pornet

Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

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Reductive Alkylation of 2,5-Dimethoxybenzoic Acid: A Direct Synthesis of Dihydrofluoren-2-ones

Summary: A two-operation procedure is described for the synthesis of 3,4-dihydrofluoren-2(1*H*)-ones from "reductive alkylation" of 2,5-dimethoxybenzoic acid with benzyl halides, followed by cyclodehydration of the adducts, with concomitant decarboxylation.

Sir: 3,4-Dihydrofluoren-2(1*H*)-ones have been employed as intermediates in syntheses of C-nor-D-homosteroids[1] and have good potential for gibberellin synthesis,[2] but published procedures for their preparation are generally long, are inefficient, and lack flexibility.[1-3] Alkylation of dianion 1 by phenethyl iodides, followed by acid-promoted cyclodehydration of the adducts has provided a very direct and flexible route to tetrahydrophenanthren-2-ones.[4] We now report an adaptation of this alkylation–cyclodehydration strategy to the synthesis of dihydrofluoren-2-ones.

Dianion 1, prepared by lithium–ammonia reduction of 2,5-dimethoxybenzoic acid, was rapidly alkylated in situ by a range of benzyl bromides, and acids **2a–e**[5] were obtained in good yield after removal of the ammonia and careful acidification to pH 5.5. Cyclization of acid **2a** in polyphosphoric acid (2 h, 25 °C) and of acid **2b** in 85%

(1) Johnson, W. S.; Cox, J. M.; Graham, D. W.; Whitlock, H. W. *J. Am. Chem. Soc.* **1967**, *89*, 4524. Battacharyya, B. K.; Bose, A. K.; Chaterjee, A.; Sen, B. P. *J. Indian Chem. Soc.* **1964**, *41*, 479. Green, M. J.; Abraham, N. A.; Fleischer, E. B.; Case, J.; Fried, J. *J. Chem. Soc., Chem. Commun.* **1970**, 234.
(2) Beames, D. J.; Mander, L. N.; Turner, J. V. *Aust. J. Chem.* **1974**, *27*, 1977.
(3) Fried, J.; Abraham, N. A. *Tetrahedron Lett.* **1965**, 3505. Ishikawa, N.; Okazaki, M. *Yuki Gosei Kagaku Kyokai Shi* **1958**, *16*, 467; *Chem. Abstr.* **1958**, *52*, 1834.
(4) Hook, J. M.; Mander, L. N.; Urech, R. *Synthesis* **1979**, 374.
(5) All compounds were obtained as crystalline solids, characterized by C and H elemental analysis (±0.3%), accurate mass measurement, and IR, ^1H NMR, and mass spectra. Percentage yields of pure, isolated products are indicated in parentheses.

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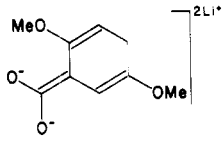
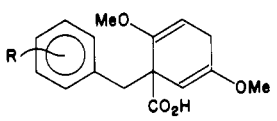
Chart I

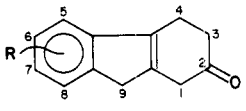


1



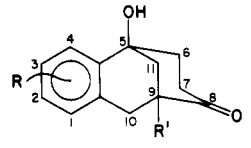
2

a R = 3-OMe (75)
b R = 3,5-$(OMe)_2$ (68)
c R = 4-OMe (77)
d R = H (74)
e R = 2-Me (74)
f R = 2-CO_2Me, 3-OMe (88)



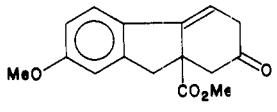
3

a R = 7-OMe (75)
b R = 5,7-$(OMe)_2$ (92)
f R = 8-CO_2Me, 7-OMe (85)

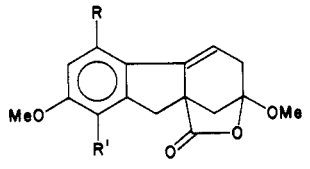


4

b R = 2,4-$(OMe)_2$, R' = CO_2H (90)
d R = H, R' = H (72)
e R = 1-Me, R' = CO_2H (85)



5



6

a R,R' = H (92)
b R = OMe, R' = H (65)
f R = H, R' = CO_2Me (62)

sulfuric acid (10 min, 25 °C)[6] proceeded smoothly to give the desired fluorenones **3a**[7] and **3b**, respectively. The brevity of this two-stage operation is in sharp contrast to the length of an earlier preparation of **3a** in 10 steps from fluorene.[3]

Similar treatment of acids **2c–e**, which lack a suitable para-activating group, did not afford fluorenones. Even under forcing conditions, **2c** was simply hydrolyzed with concomitant decarboxylation to give 2-(4-methoxybenzyl)cyclohexane-1,4-dione. Acids **2d** and **2e**, however, gave the 5,9-methanobenzocyclooctene derivatives **4d** and **4e**, respectively. Clearly, the failure of **2d** and **2e** to form fluorenones points up a limitation of the present approach,[8] but the formation of the bicyclo[3.3.1]nonane ring system was not surprising. 1-Benzylcyclohexanols form this skeleton, rather than the more strained hexahydrofluorenes,[9] and molecular models reveal that the transition state leading to the caged product possesses the more favorable reaction geometry. It seemed likely that bicyclononanes might also be formed from **2a** and **2b**, and when the latter was treated with 1 M HCl–acetone for 1 h at 25 °C, acid **4b** was obtained in 90% yield. The assignment of structure to **4b** was supported by its resistance to dehydration and its ease of decarboxylation (at its melting point, ~170 °C). Treatment of acid **4b** with 85% sulfuric acid (70 min, 25 °C) afforded hydrofluorenone **3b** as the sole product. It seems likely, therefore, that the bicyclononane derivatives are kinetically favored in all cases, but that a methoxyl substituent on the aromatic ring facilitates reprotonation and thence retrocyclization. When the hexahydrofluorene skeleton is formed, dehydration may occur readily, effectively inhibiting retrogression and leading to an accumulation of the desired ketones **3a** and **3b**. Decarboxylation may occur at a number of stages in the complex equilibria involved.

The main motivation in developing the current procedures arose from our interest in developing an efficient preparation of the ester **3f** for a projected gibberellin synthesis.[2] The intermediate acid **2f** was obtained readily from reaction of dianion **1** with methyl 6-(iodomethyl)-2-methoxybenzoate[10] (although this time it was necessary to alkylate in tetrahydrofuran solution after removal of the ammonia), and cyclization in polyphosphoric acid (5 h, 25 °C) smoothly afforded the desired fluorenone **3f**. Of further interest to possible gibberellin syntheses was the retention of the angular carboxyl function.[11] This was readily achieved through methylation (diazomethane) prior to cyclization (85% sulfuric acid, 30 min, 25 °C), e.g., **2a** → **5**,[12] or by boron trifluoride etherate–dichloromethane treatment (1 h, 25 °C) of the acids **2a,b,f** to give the corresponding lactones **6a,b,f**, respectively.

The work described herein is a further demonstration of the potential in "reductive alkylation" of aromatic acids for very direct carbocyclic syntheses.[14] The acid dianions such as **1** serve, in effect, as more accessible and reactive operational equivalents to the traditional anions derived from the analogous β-keto esters.[13]

Acknowledgment. We thank V. Richardson for her very competent technical assistance.

Registry No. **1**, 70887-37-5; **2a**, 73177-38-5; **2b**, 73177-39-6; **2c**, 73177-40-9; **2d**, 73177-41-0; **2e**, 73177-42-1; **2f**, 73177-43-2; **3a**, 5043-53-8; **3b**, 73177-44-3; **3f**, 73177-45-4; **4b**, 73177-46-5; **4d**, 73177-47-6; **4e**, 73192-73-1; **6a**, 73177-48-7; **6b**, 73177-49-8; **6f**, 73177-50-1; methyl 6-(iodomethyl)-2-methoxybenzoate, 73177-51-2; 3-methoxybenzyl

(6) Of the standard range of cyclodehydration reagents, these two reagents gave the best results. However, one system usually gave significantly better yields than the other for any given substrate.

(7) The melting point and mixture melting point [mp and mmp 87–89 °C (lit.[3] mp 89–91 °C)], IR, ^1H NMR, and TLC were identical with those of an authentic sample.

(8) The incorporation of a suitably located activating group such as methoxyl should ensure cyclization to the fluorene-based skeleton.

(9) Cook, J. W.; Hewitt, C. L. *J. Chem. Soc.* **1936**, 62. Barnes, R. A.; Sedlak, M. *J. Org. Chem.* **1962**, *27*, 4562.

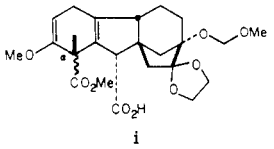
(10) This compound was formed in 84% yield from the chloride (sodium iodide, acetone, 1.5 h, 25 °C) which had been prepared by an adaptation of the elegant procedure of: Dean, R. T.; Rapoport, H. *J. Org. Chem.* **1958**, *43*, 2115. Thus, metalation of *N,N*-dimethyl-3-methoxybenzylamine (*n*-butyllithium, ether, 20 h, 25 °C) and acylation with dimethyl carbonate gave methyl 6-[(dimethylamino)methyl]-2-methoxybenzoate (90% yield) which on treatment with methyl chloroformate (tetrahydrofuran, 16 h, 25 °C) gave the benzyl chloride (95% yield). The direct literature method gave material containing 10% of a regioisomer.

(11) Strategies for gibberellin syntheses based on this type of intermediate have been reviewed: Fujita, E. *Heterocycles* **1977**, *7*, 709.

(12) This unstable ketone was purified and characterized as its ethylene ketal. The corresponding ethyl ester has been prepared.[13]

(13) Thompson, H. W. *J. Org. Chem.* **1971**, *36*, 2577.

(14) To date the shortest synthesis of a natural gibberellin takes 36 steps.[15] Ester **3f** has recently been converted (Hook, J. M.; Urech, R. unpublished results) by established methodology[2,16] into the advanced intermediate (i) in ca. 10 steps. The efficient synthesis of fluorenone **3f** therefore provides the potential for very much shorter sequences leading to synthetic gibberellins.



i

(15) Corey, E. J.; Danheiser, R. L.; Chandrasekaran, S.; Keck, G. E.; Gopalan, B.; Larsen, S. D.; Siret, P.; Gras, J.-L. *J. Am. Chem. Soc.* **1978**, *100*, 8034.

(16) Loewenthal, H. J. E.; Schatzmiller, S. *J. Chem. Soc., Perkin Trans. 1* **1976**, 944 and references cited therein.

bromide, 874-98-6; 3,5-dimethoxybenzyl bromide, 877-88-3; 4-methoxybenzyl bromide, 2746-25-0; benzyl bromide, 100-39-0; 2-methylbenzyl bromide, 89-92-9.

James M. Hook, Lewis N. Mander*

Research School of Chemistry
Australian National University
Canberra, ACT 2600, Australia

Received October 30, 1979

Naphthalenes and Biphenyls via a Novel Reaction of *N,N*-Dimethylformamide Dimethyl Acetal

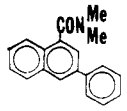
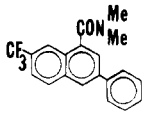
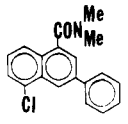
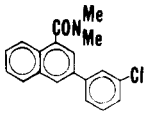
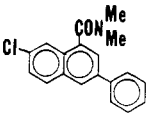
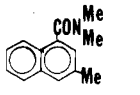
Summary: In the presence of *N,N*-dimethylformamide dimethyl acetal at elevated temperatures, certain methylene ketones react to form *N,N*-dimethyl-1-naphthalenecarboxamides, while diketones react to form *N,N,O*-trimethylsalicylamides.

Sir: Since the initial report by Meerwein et al. on the synthesis and properties of formamide acetals[1] and their development for use as alkylating and formylating agents,[2] numerous transformations of organic substrates employing these compounds have appeared in the literature.[3] We report here an unusual conversion effected on certain substituted acetone derivatives by *N,N*-dimethylformamide dimethyl acetal (A) which affords aromatic rings as end products.

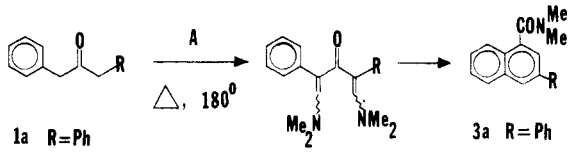
Our initial aim was the conversion of 1,3-diphenylacetone (**1a**) to the bis-enaminone **2a** by treatment with acetal A.[4] Indeed, **2a** may be formed from **1a** in good yields (70–75% as a mixture of *E* and *Z* components) at reaction temperatures of 110–112 °C (reflux with neat A). However, when we treated **1a** with acetal A at 150–200 °C in a steel autoclave under nitrogen, we obtained in greater than 90% yield[5] compound **3a**: $C_{19}H_{17}NO$ (combustion analysis: C, 82.45; H, 6.08; N, 5.48); mp 136–138 °C.[6] An X-ray crystallographic analysis[7] established the structure of **3a** to be *N,N*-dimethyl-3-phenyl-1-naphthalenecarboxamide. Spectrographic data were consistent with this structure.

The conversion of **1** to **3** represents a novel transformation of 1,3-diaryl- and 1-aryl-3-alkylacetones to naphthalene derivatives (Scheme I), which upon further examination has been shown to be general[8] (Table I). It appears that the reaction proceeds by the intervention of intermediates such as **2**.[10]

Table I

(1) R	(3)	% Yield	mp °C
a. 	a. 	95	136–138
b. 	b. 	50[9]	107–108
c. 	c. 	8.9	113–115
	d. 	0.89	142–143
	e. 	1.1	145–147
d. Me	f. 	90	74–76

Scheme I



In an effort to delineate the scope of this reaction, we performed experiments on the diketones **1e** and **1f**. Treatment of either **1e** or **1f**[11] (Scheme II) with acetal A did not give naphthalenes but instead afforded in moderate yields the 4-methoxybiphenyl-3-carboxamides **4a** and **4b**, respectively. The structure of **4a** was established by an alternate synthesis from authentic methyl 4-hydroxybiphenyl-3-carboxylate (Scheme II).[12] No benzenoid nucleus could be isolated, however, from the reaction of acetalacetone with A at 180 °C. At lower temperatures, the expected enaminedione was formed.

We also observed aromatic ring formation upon treatment of (phenoxyacetyl)diethylstyrylamine (**5**)[4] with A at 180 °C. The phenoxynaphthylamide **3g** was isolated after column chromatography (silica gel, 25% EtOAc/toluene) as a glass in 26% yield. In a similar manner, 1-phenoxy-2,4-pentanedione (**6**)[13] was converted to the phenoxy-

(1) H. Meerwein, P. Borner, O. Fuchs, H. J. Sasse, H. Schrodt, and J. Spille, *Chem. Ber.*, **89**, 2060 (1956); H. Meerwein, W. Florian, N. Schön, and G. Stopp, *Justus Liebigs Ann. Chem.*, **641**, 1 (1961).

(2) H. Bredereck, F. Effenberger, and G. Simchen, *Angew. Chem.*, **73**, 493 (1961); H. Bredereck, G. Simchen, S. Rebsdat, W. Kantlehner, P. Horn, R. Wahl, H. Hoffmann, and P. Grieshaber, *Chem. Ber.*, **101**, 41 (1968).

(3) R. F. Abdulla and R. S. Brinkmeyer, *Tetrahedron*, **35**, 1675–1735 (1979).

(4) R. F. Abdulla, T. L. Emmick, and H. M. Taylor, *Synth. Commun.*, **7**, 305 (1977); R. F. Abdulla, K. H. Fuhr, and H. M. Taylor, *ibid.*, **7**, 313 (1977).

(5) These refer to *isolated* yields of *chromatographically homogeneous* materials.

(6) **3a**: M^+ *m/e* 275; IR (Nujol) $\tilde{\nu}$ 1635 (C=O, amide) cm^{-1}; NMR ($CDCl_3$) δ 7.1–8.1 (m, 12 H), 2.8 (s, 3 H), 3.2 (s, 3 H), T_c = 90 °C (s, 6 H); UV λ_{max}^{EtOH} (ϵ) 211 (36 756), 253 (52 267), 288 (11 330) nm. All of the compounds reported in this communication were fully characterized by satisfactory combustion analysis and spectrography.

(7) X-ray analysis was performed by Drs. N. D. Jones and M. O. Chaney of the Physical Chemistry Research Department of Eli Lilly and Co.

(8) One vacant ortho position on one aromatic ring of the substituted acetone is a necessary condition for naphthalene formation.

(9) Other isomers were detected by NMR spectroscopy in the crude reaction product, but their isolation by column chromatography proved unsuccessful.

(10) This conclusion is based on the cyclization of **2a** (R = Ph) upon thermolysis at 200 °C under nitrogen in a stainless steel autoclave.

(11) **1e** and **1f** were prepared by using sodium amide/dry ether in a Claisen condensation of acetone with ethyl phenylacetate and with ethyl [*m*-(trifluoromethyl)phenyl]acetate, respectively. See also H. Mühlemann, *Pharm. Acta Helv.*, **24**, 356 (1949), for the synthesis of **1e**.

(12) Obtained from the Organic Compounds File of Eli Lilly and Co.

(13) This material was prepared by Claisen condensation of acetone with methyl phenoxyacetate in a manner analogous to that of ref 11 in 61.5% yield; bp 92–94 °C (0.5 mm).

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