# A New Procedure for Regiospecific Syntheses of Benzopyran-1-ones

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A new, general route to benzopyran-1-ones **33** from phthalaldehydic acids **27** and nitroalkanes **28** is described. The sequence permits straightforward variation of both the 3-substituent and the pattern of functionalization on the aromatic ring of the benzopyran ring system. The (nitroalkyl)isobenzofuranones **29** obtained from condensation of **27** and **28** with triethylamine in DMSO were converted to 2-(2-nitroalkyl)benzoic acids **30** with sodium borohydride in DMSO. Nef reactions on **30** furnished the carboxy ketals **32**, which on intramolecular cyclization and dehydration gave the objective benzopyran-1-ones **33**. The sequence can be abbreviated, such that purifications of only the (nitroalkyl)isobenzofuranones **29** and the final benzopyranones **33** are necessary.

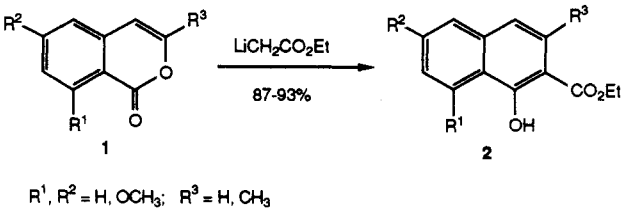
A wide variety of benzopyran-1-ones occur naturally, and the ring system also occurs as a structural fragment in many other natural products.[1] Because it is useful as an intermediate to other heterocyclic and carbocyclic compounds,[2] the ring system has been of specific interest to our synthetic program in polycyclic aromatic natural products. We have demonstrated previously, as shown in Scheme I, that the lithium enolate of ethyl acetate reacts smoothly with benzopyran-1-ones **1** to give naphthoates **2** in high yield.[3,4] In conjunction with our planned use of this reaction to prepare polycyclic natural products with a naphthalene fragment,[5] we needed an efficient, general benzopyran-1-one synthesis that would be regiospecific and permit straightforward variation of the 3-substituent and also the substitution pattern on the benzenoid ring. An additional requirement was that the protocol be sufficiently mild that functional groups elsewhere in the molecule would be unaffected.

There are numerous synthetic procedures to benzopyran-1-ones.[1b,c] One of the most general, the acylation of homophthalic anhydrides **3** with anhydrides **4** using an amine catalyst, is shown in Scheme II.[6] The initial acylation product **5** can be converted to the objective benzopyranone **6** either by heating with concentrated sulfuric acid or through hydrolysis and decarboxylation to the keto acid **7**, which is then intramolecularly dehydrated. This route to benzopyran-1-ones is practical only when the anhydride is relatively inexpensive, since it must be used in large excess and only half the acyl component of the anhydride is used. Substitution of aliphatic acid chlorides for the corresponding anhydrides invariably gave low yields of the acetylated product.[7] However, reasonable yields have been obtained with aryl acid chlorides.

Stobbe condensations of homophthalates **8** with aldehydes **9** have also been widely employed for synthesis of benzopyran-1-ones **6** as shown in Scheme III. Reactions of the homophthalate **8** with aromatic aldehydes gave good yields of the the styryl half esters **10**; however, the corresponding reaction with aliphatic aldehydes gave low yields.[8] The additional steps necessary to convert **10** to **6** are harsh, and the overall yields of products using this approach are rather modest, especially for benzopyranones containing a 3-alkyl group.

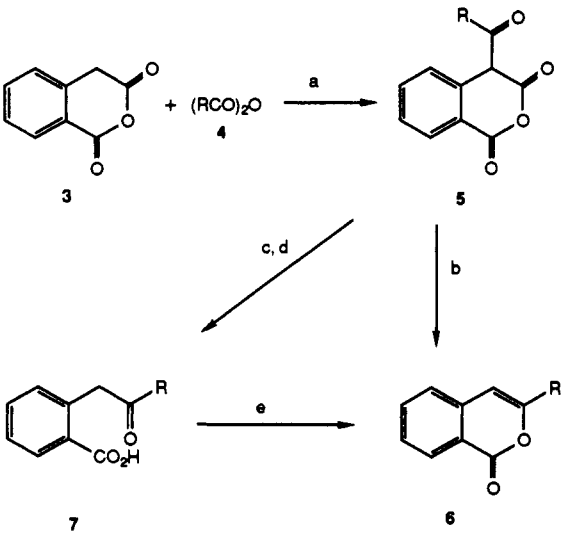
Direct and indirect procedures that provide benzopyran-1-ones from benzoic and *o*-toluic acid derivatives, via the intermediacy of carbanions, have been reported, and three such examples are shown in Scheme IV. Ring metalation ortho to the amide in **14**, followed by reaction with the epoxide **15**, gave the 3,4-dihydrobenzopyran-1-one **16** in 35% yield.[9] Deprotonation of the methyl group in

**Scheme I**




$R^1, R^2 = H, OCH_3$; $R^3 = H, CH_3$

**Scheme II**[a]




[a] (a) Py; (b) $H_2SO_4$; (c) NaOH; (d) $H_3O^+$; (e) $(CH_3CO)_2O$ or $\Delta$.

(1) (a) Johnston, H. W.; Kaslow, C. E.; Langsjoen, A.; Shriner, R. L. *J. Org. Chem.* **1948**, *13*, 477. (b) Barry, R. D. *Chem. Rev.* **1964**, 229. (c) Livingstone, R. In *Rodd's Chemistry of Carbon Compounds*; Coffey, S., Ed.; Elsevier: New York, 1977; Vol. IV, Part E, pp 290-297.

(2) (a) Muller, E. *Chem. Ber.* **1909**, *42*, 423. (b) Jones, J. B.; Pinder, A. R. *J. Chem. Soc.* **1958**, 2612. (c) Kanevskaya, S. I.; Malinina, S. I. *J. Gen. Chem. (USSR)* **1956**, *25*, 727. (d) Ribbens, C. *Sci. Commun. Res. Dept., N. V. Koninkl. Pharm. Fabrieken v/h Brocades-Stheeman Pharmacia*, **1960-1961**, *10*, 9.

(3) Hauser, F. M.; Pogany, S. A. *J. Heterocycl. Chem.* **1978**, *15*, 1535.

(4) Hauser, F. M.; Rhee, R. P. *J. Org. Chem.* **1977**, *42*, 4155.

(5) For an alternate procedure, see: Hauser, F. M.; Rhee, R. P. *J. Org. Chem.* **1978**, *43*, 178.

(6) (a) Tirodkar, R. B.; Usgaonkar, R. N. *J. Ind. Chem. Soc.* **1969**, *46*, 10. (b) Nadkarne, D. R.; Usgaonkar, R. N. *Indian J. Chem.* **1978**, *16B*, 320. (c) Tirodkar, R. B.; Usgaonkar, R. N. *Curr. Sci.* **1972**, *41*, 701. (d) Hauser, F. M.; Rhee, R. *J. Am. Chem. Soc.* **1977**, *99*, 4533.

(7) Schnekenburger, J. *Arch. Pharm. (Weinheim, Ger.)* **1965**, *298*, 4.

(8) (a) Loewenthal, H. J. E.; Pappo, R. *J. Chem. Soc.* **1952**, 4799. (b) Yamato, M.; Hashigaki, K. *Chem. Pharm. Bull. (Tokyo)* **1976**, *24*, 200. (c) Naoi, Y.; Higuchi, S.; Ito, H.; Nakano, T.; Sakai, K.; Matsui, T.; Wagatsums, A.; Nishi, A.; Sano, S. *Org. Prep. Proc. Int.* **1975**, *7*, 129. (d) Kobayashi, T. *Sci. Rep. Tohoku Imp. Univ., First Ser.* **1942**, *32*, 73; *Chem. Abstr.* **1950**, *44*, 4013*f*.

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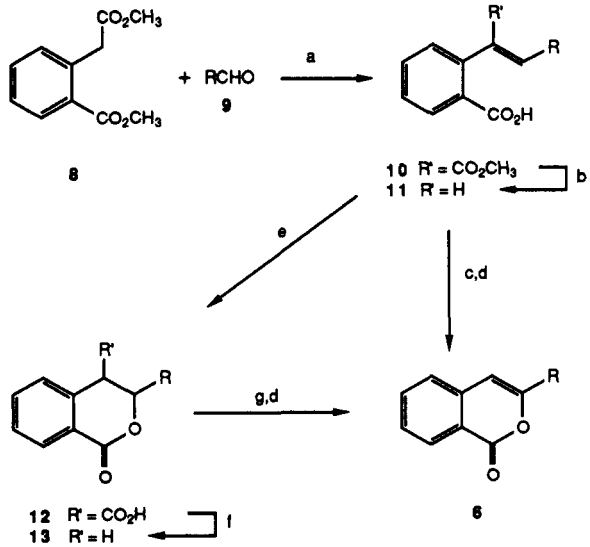
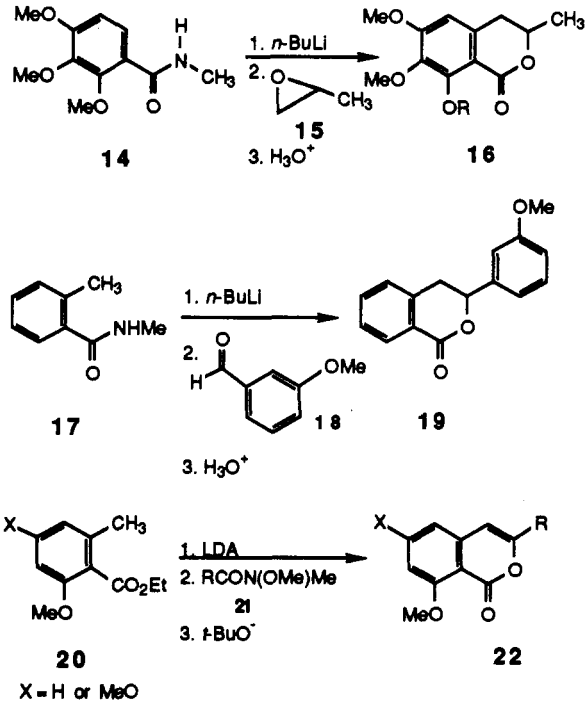
**Scheme III**[a]



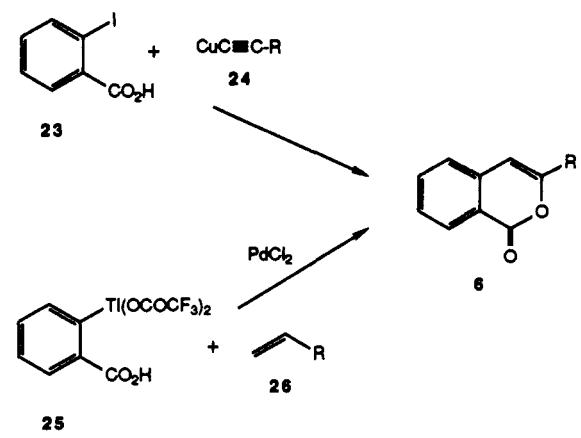
[a] (a) NaH; (b) NaOH, DMF, Δ; (c) $Br_2$; (d) Py; (e) $H_2SO_4$; (f) $AlBr_3$; (g) NBS.

**Scheme IV**



the *o*-toluamide **17**, followed by reaction of the anion with the benzaldehyde **18**, gave the 3-phenyl-3,4-dihydrobenzopyran-1-one **19** in 13% yield.[10] This approach was unsuccessful when aliphatic aldehydes were used. Recently, Staunton et al.[11] reported that the *o*-toluate anion prepared from **20** can be condensed with *N*-methoxy-*N*-methylamides **21** in moderate yield, and the resultant keto esters can be cyclized to the benzopyran-1-ones **22**. A methoxyl group ortho to the ester functionality is essential, in order to prevent dimerization of the toluate anion.[12]

**Scheme V**



Here again, yields declined when the amide component was aliphatic.

Two recently developed routes that utilize organometallic intermediates are shown in Scheme V. The coupling of *o*-iodobenzoic acid (**23**) with copper acetylides **24**[13] and of the ortho thallated benzoic acid **25** with terminal olefins **26** using palladium chloride[14] furnish benzopyranones **6**. Although both are potentially general procedures, the use of more highly functionalized benzoic acid derivatives has not been described.

The lack of flexibility, harsh conditions, and overall inefficiency of existing methods for preparing 3-alkylbenzopyran-1-ones led us to devise a new, general route to this ring system, and this is shown in Scheme VI. The sequence, accomplished from phthalaldehydic acids **27** and nitroalkanes **28** allows straightforward variation of both the 3-substituent and the pattern of functionalization on the aromatic ring. The reaction conditions are mild, and special precautions such as the use of anhydrous conditions are unnecessary. The sequence can be abbreviated, such that only two products require purification; the (nitroalkyl)isobenzofuranones **29** and the final benzopyran-1-one **33**. In contrast to other methods, this procedure provides good yields of 3-alkyl-substituted isobenzofuranones.

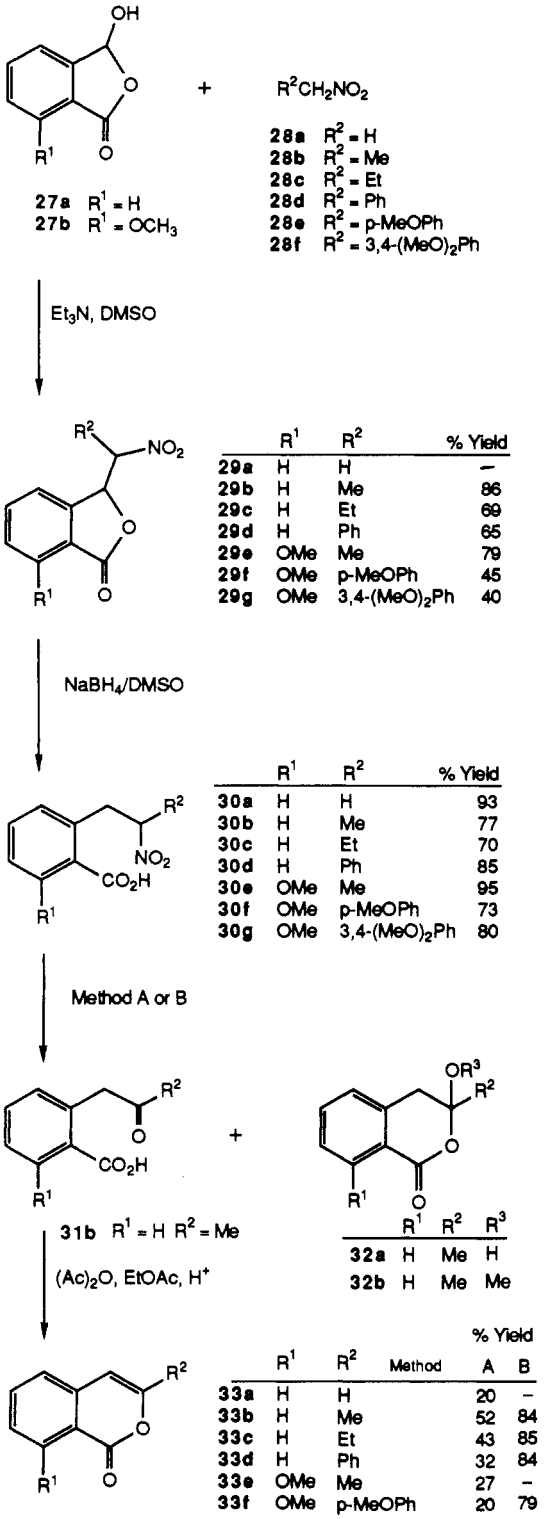
The synthetic plan was based upon the expectation that nitroalkyl-substituted isobenzofuranones **29** from Henry condensation of nitroalkanes **28** with phthalaldehydic acids **27** could be converted to the 2-nitroalkyl acids **30** through reductive elimination. Subsequent transformation of the nitromethylene in **30** to a carbonyl group would give the keto acids **31**, which on intramolecular cyclization and dehydration would yield the objective benzopyran-1-ones **33**.

There are several literature reports describing the condensation of phthalaldehydic acids with nitroalkanes.[15] Reductive conversion of β-acetoxy nitro compounds to nitroalkanes is also known,[16] but application of this reaction to (nitroalkyl)isobenzofuranones such as **29** had not been reported. Likewise, conversion of 2-(2-nitroalkyl)-benzoic acids **30** to keto acids **31** had not been described.

The literature conditions for Henry condensation of phthalaldehydic acid with nitro compounds was examined initially. Condensation of phthalaldehydic acid (**27a**) with

(9) Bhide, B. H.; Gupta, V. P.; Narasimhan, N. S.; Mali, R. S. *Chem. Ind.* **1975**, 519.
(10) Govindachari, T. R.; Parthasarathy, P. C.; Desai, H. K.; Ramachandran, K. S. *Indian. J. Chem.* **1975**, *13*, 537.
(11) Lewis, C. N.; Spargo, P. L.; Staunton, J. *Synthesis* **1986**, 944.
(12) Hauser, F. M.; Rhee, R. P.; Prasanna, S.; Weinreb, S. M.; Dodd, J. H. *Synthesis* **1980**, 72.
(13) Batu, G.; Stevenson, R. *J. Org. Chem.* **1980**, *45*, 1532.
(14) Larock, R. C.; Varaprath, S.; Lau, H. H.; Fellows, C. A. *J. Am. Chem. Soc.* **1984**, *106*, 5274.
(15) (a) Whelton, B. D.; Huitric, A. C. *J. Org. Chem.* **1970**, *35*, 3143. (b) Beke, D.; Szantay, C. *Arch. Pharm. (Weinheim, Ger.)* **1958**, *291/63*, 342. (c) Wilson, J. W., III; Zirkle, C. L.; Anderson, E. L.; Stehle, J. J.; Ullyot, G. E. *J. Org. Chem.* **1951**, *16*, 792.
(16) Bachman, G. B.; Maleski, R. J. *J. Org. Chem.* **1972**, *37*, 2810.

**Scheme VI**[a]




[a] Method A: (a) NaOMe, MeOH; (b) $TiCl_3$, $NH_4OAc$; (c) $H_3O^+$. Method B: (a) NaOH; (b) $H_2SO_4$, MeOH.

nitromethane (**28a**) employing sodium hydroxide in methanol[15a] gave the (nitromethyl)isobenzofuranone **29a** in 81% yield. Nitroethane (**28b**) also worked reasonably well, providing **29b** in 60% yield after 2 days. When nitropropane (**28c**) was employed under the same conditions, the yield of adduct was only 38% after 5 days, and phenylnitromethane[17] (**28d**) failed to react.

(17) Hauser, F. M.; Baghdanov, V. M. *J. Org. Chem.*, in press.

The modest yield of adduct from nitropropane (**28c**) and the failure of phenylnitromethane (**28d**) to furnish a product led us to examine other bases and solvent systems for the condensation. Ultimately, triethylamine in dimethyl sulfoxide was found to be the best. Condensation of phthalaldehydic acid (**27a**) with nitroethane (**28b**), nitropropane (**28c**), and phenylnitromethane (**28d**), under these conditions, gave the (nitroalkyl)isobenzofuranones **29b–d** in 86, 69, and 65% yields, respectively. Triethylamine was too weak a base to deprotonate nitromethane (**28a**), and in that case, sodium hydroxide in methanol provided the best yield of the (nitromethyl)isobenzofuranone (**29a**). In all cases where diastereoisomers were possible (**29b–d**, R = Me, Et, Ph), mixtures were formed. Although most of the isomers could be readily separated by crystallization or chromatography, the mixtures were usually used in subsequent steps.

In order to explore the effect of an aromatic methoxyl substituent, the reaction was performed with 7-methoxyphthalaldehydic acid[18] (**27b**). Condensation of **27b** with nitroethane (**28b**), (4-methoxyphenyl)nitromethane[17] (**28e**), and (3,4-dimethoxyphenyl)nitromethane[17] (**28f**) gave the (nitroalkyl)isobenzofuranones **29e–g** in 40–79% yield. Although condensation of **27a** with phenylnitromethane gave good results, condensation of **27b** with methoxy-substituted phenylnitromethanes gave modest yields of products.

Reductive cleavage of the (nitroalkyl)isobenzofuranones **29** to the (nitroalkyl)benzoic acids **30** was accomplished in a straightforward manner. Treatment of **29** with sodium borohydride in dimethyl sulfoxide consistently provided the (nitroalkyl)benzoic acids **30** in 70–95% yield.[16]

Conversion of the nitro functionality to a carbonyl group initially proved to be troublesome. McMurry's titanium trichloride procedure[19] was examined first. A $^1H$ NMR spectrum showed that the product from reduction of **30b** was a mixture of the keto acid **31b**, the hemiacetal **32a**, and the benzopyran-1-one **33b**. In order to quantitate the reaction, the initially received mixture was cyclized directly to the benzopyran-1-one **33b** with acetic anhydride in ethyl acetate using perchloric acid as a catalyst.[20] Application of this procedure to the remaining nitro acids **30** furnished the benzopyran-1-ones **33a–f** in 20–52% yields.

Concurrently, we examined the oxidative hydrolysis of nitroalkanes to carbonyl compounds with hydrogen peroxide and potassium carbonate.[21] This procedure did, after cyclization, yield some benzopyran-1-one **33b** from the nitro acid **30b**, but again the yields were erratic and low. Our finding that the quantity of hydrogen peroxide used in the reaction had no effect on the yield led us to suspect that hydrogen peroxide was not essential for reaction. This supposition was confirmed when experiments with and without hydrogen peroxide gave similar yields of the benzopyran-1-one **33b**.

This result suggested that a simple Nef[22] reaction was occurring, and our further studies focused on using this type of procedure to convert the nitro acids **30** to the keto acids **31**. Utilizing a modified Nef reaction,[23] the anion of **30b** was generated with sodium methoxide in methanol,

(18) Prepared through hydrolysis of the phenylthioacetal described in ref 12.
(19) McMurry, J. E.; Melton, J. *J. Org. Chem.* **1973**, *38*, 4367.
(20) Edwards, B. E.; Rao, P. N. *J. Org. Chem.* **1966**, *31*, 324.
(21) Olah, G. A.; Arvanaghi, M.; Vankar, Y. D.; Prakash, G. K. S. *Synthesis* **1980**, 662.
(22) (a) Noland, W. E. *Chem. Rev.* **1955**, 137. (b) Van Tamelen, E. E.; Theide, R. J. *J. Am. Chem. Soc.* **1952**, *74*, 2615. (c) Hawthorne, M. F. *J. Am. Chem. Soc.* **1957**, *79*, 2510. (d) Sun, S. F.; Folliard, J. T. *Tetrahedron* **1971**, *27*, 323.
(23) Jacobson, R. M. *Tetrahedron Lett.* **1974**, 3216.

which was then added to sulfuric acid in methanol. The product, by $^1H$ NMR spectroscopy, was principally the carboxy ketal **32b**. Treatment of this material with perchloric acid and acetic anhydride in refluxing ethyl acetate[20] furnished 3-methylbenzopyranone **33b** in 84% yield. The characteristic sky-blue color,[22b-d] which is formed on addition of the nitronate anion to the acid solution, was used to follow the progress of the hydrolysis. The disappearance of the blue color indicated that the reaction was complete.

The procedure also worked well if the nitronate anion was generated in aqueous sodium hydroxide or in a solution of aqueous sodium hydoxide and methanol. Application of this procedure to the other nitro acids **30** gave the benzopyran-1-ones **33** in 79–85% yield. Workup was straightforward, and the products were readily isolated in pure form. While this procedure worked well for the preparation of benzopyran-1-ones with a 3-substituent, the unsubstituted benzopyran-1-one **33a** proved to be an exception.

Once the individual steps had been established, it proved possible to abbreviate the sequence such that only two steps were needed to prepare the benzopyran-1-ones **33**. Instead of isolating the nitroacids **30b,c,e** from sodium borohydride reduction of the nitroalkyl isobenzofuranones **29b,c,e**, aqueous sodium hydroxide was added to the dimethyl sulfoxide solution of the nitro acids to ensure anion formation. The anion solution was then slowly added to sulfuric acid in methanol at 0 °C. Once the blue color disappeared (1–2 h), the Nef product was extracted with ethyl acetate. Treatment of the ethyl acetate solution with perchloric acid and acetic anhydride at reflux for 1–2 h gave the benzopyran-1-ones (**33b,c,e**) in 65–85% yield. The abbreviated sequence produced higher yields, was more efficient, and allowed for three steps to be performed without purification of intermediates.

In summary, a new and reasonably efficient method for syntheses of benzopyran-1-ones from phthalaldehydic acids and nitro compounds has been developed. It is especially useful for the synthesis of 3-alkyl-substituted isobenzofuranones. A modification of this sequence permitted preparation of benzopyran-1-ones in only two steps. The Nef reaction requires substrates that are stable to moderate acidity, but other than that, no other severe conditions were required. The methodology is straightforward, and the yields were generally good.

## Experimental Section

**General Procedures.** Melting points were taken on a Kofler hot-stage microscope and are uncorrected. IR spectra were recorded on a Perkin-Elmer FT-1800 infrared spectrophotometer and are expressed in wave numbers. Proton and $^{13}C$ NMR spectra were recorded on a JEOL FX90Q spectrometer. Chemical shifts are reported as $\delta$ values in ppm relative to TMS. EI (70 eV) and FAB mass spectra were obtained with a VG 7070E spectrometer. Analytical thin-layer chromatography plates (silica gel 60 F-254, layer thickness 0.25 mm) were manufactured by E. Merck and Co. Silica gel for column chromatography utilized E. Merck silica gel 60, 70–230 mesh ASTM. Radial thick-layer chromatography was performed on a chromatotron (Harrison Research) with plates (2 and 4 mm thickness) made with silica gel from E. Merck (60, PF-254). Carbon, hydrogen, and nitrogen analyses were performed by Galbraith Laboratories, Knoxville, TN. Triethylamine and DMSO were distilled from $CaH_2$. Hexanes, $CH_2Cl_2$, and EtOAc used for chromatography were distilled.

**3-(Nitromethyl)-1(3*H*)-isobenzofuranone (29a).** The procedure of Wheatton and Huitric[15a] was employed. Aqueous sodium hydroxide (10 N, 8.4 mL, 84 mmol) was slowly added to a chilled (0 °C) solution of phthalaldehydic acid (**27a**) (5.00 g, 33.3 mmol) and nitromethane (**28a**) (2.2 mL, 40 mmol) in methanol (50 mL). The solution was allowed to warm to room temperature and then stirred for 2.5 h. Acetic acid (5 mL) and then hydrochloric acid (60 mL, 6 N) were added, and the resulting mixture was chilled (0 °C). Filtration of the precipitate gave 5.2 g (81%) of **29a** as white crystals. A sample recrystallized from methylene chloride–hexanes had mp 126–128 °C (lit.[15a] mp 129–131 °C): $^1H$ NMR ($CDCl_3$) $\delta$ 4.75 (dd, 1 H, $J$ = 7.04 Hz, $J$ = 14.08 Hz, C*H*$NO_2$), 4.80 (dd, 1 H, $J$ = 4.84 Hz, $J$ = 14.08 Hz, C*H*$NO_2$), 6.15 (dd, 1 H, $J$ = 4.84 Hz, $J$ = 7.04 Hz, Ar C*H*), 7.44–8.08 (m, 4 H, Ar *H*).

**General Procedure for Nitro Aldol Condensations.** The phthalaldehydic acid **27** (6 mmol), the nitro compound **28** (1.4 equiv), and triethylamine (1.6 equiv) in DMSO (6 mL) were stirred at room temperature for 1–2 days. The reaction was quenched with acetic acid (0.8 mL), acidified with hydrochloric acid (12 N, 3 mL), and stirred for 30–60 min. Brine (25 mL) was added, and the resulting mixture extracted with ethyl acetate (2 × 50 mL). The combined organic solutions were washed with brine (4 × 20 mL), dried ($MgSO_4$), filtered, and evaporated at reduced pressure. Chromatography of the residue on silica gel (20 g, $CH_2Cl_2$) or recrystallization furnished the pure (nitroalkyl)isobenzofuranones **29**.

**3-(1-Nitroethyl)-1(3*H*)-isobenzofuranone (29b).** The nitro lactone **29b**, prepared from phthalaldehydic acid (**27a**) and nitroethane (**28b**), was isolated in 86% yield as an oil, which solidified on standing. A $^1H$ NMR spectrum indicated a mixture of diastereoisomers: $^1H$ NMR ($CDCl_3$) $\delta$ 1.46 (d, 3 H, $J$ = 6.59 Hz, C*H*$_3$) (major isomer), 1.67 (d, 3 H, $J$ = 7.04 Hz, C*H*$_3$) (minor isomer), 4.80–5.16 (m, 1 H, C*H*$NO_2$), 6.13 (d, 1 H, $J$ = 3.96 Hz, Ar C*H*), 7.48–8.06 (m, 4 H, Ar *H*); $^{13}C$ NMR ($CDCl_3$) $\delta$ (11.9, 14.4, *C*$H_3$), 79.3, (*C*H$NO_2$), (83.0, 83.3, Ar *C*H), (123.1, 123.9), 125.8, 130.2, (134.4, 134.8), (143.8, 144.7), (168.6, 168.9, *C*=O); IR (film, $cm^{-1}$) 1772 (C=O), 1557, 1362 ($NO_2$); $m/z$ 161 ($M^+ - NO_2$, 13), 160 (75), 133 (100), 105 (25).

**3-(1-Nitropropyl)-1(3*H*)-isobenzofuranone (29c).** The nitro lactone **29c**, prepared from phthalaldehydic acid (**27a**) and nitropropane (**28c**), was isolated in 69% yield as an oil, which crystallized on standing. Recrystallization ($CH_2Cl_2$–hexanes) of the material gave a single diastereoisomer as white needles with mp 76–79 °C: $^1H$ NMR ($CDCl_3$) $\delta$ 1.07 (t, 3 H, $J$ = 7.3 Hz, C*H*$_3$), 1.80–2.42 (m, 2 H, C*H*$_2$), 4.60–4.88 (m, 1 H, C*H*$NO_2$), 5.83 (d, 1 H, $J$ = 6.2 Hz, Ar C*H*), 7.48–8.04 (m, 4 H, Ar *H*); $^{13}C$ NMR ($CDCl_3$) $\delta$ 10.1, 23.8, 78.8, 90.2, 123.0, 126.2, 126.3, 130.4, 134.4, 143.9, 168.5 (C=O); IR (film, $cm^{-1}$) 1773 (C=O), 1557, 1375 ($NO_2$); $m/z$ 175 ($M^+ - NO_2$, 14), 174 (50), 159 (20), 146 (6), 133 (100). Anal. Calcd for $C_{11}H_{11}O_4N$: C, 59.72; H, 5.01; N, 6.33. Found: C, 59.60; H, 5.08; N, 6.29.

**3-(Phenylnitromethyl)-1(3*H*)-isobenzofuranone (29d).** The nitro lactone **29d** was prepared from phthalaldehydic acid (**27a**) and phenylnitromethane (**28d**). The initial product was recrystallized ($CH_2Cl_2$–hexanes) to give **29d** in 65% yield as white crystals with mp 148–151 °C (lit.[15a] mp 157–162 °C): $^1H$ NMR ($CDCl_3$) $\delta$ 5.36 (d, 1 H, $J$ = 10.11 Hz, C*H*$NO_2$), 6.19 (d, 1 H, $J$ = 7.03 Hz, Ar *H*), 6.39 (d, 1 H, $J$ = 10.11 Hz, Ar C*H*), 7.24–7.68 (m, 7 H, Ar *H*), 7.80–8.00 (m, 1 H, Ar *H*); $^{13}C$ NMR ($CDCl_3$) $\delta$ 92.3, 123.4, 127.7, 128.0, 129.1, 129.7, 132.6, 133.8, 134.9, 138.5, 172.3 (C=O); IR (film, $cm^{-1}$) 1773 (C=O), 1560, 1367 ($NO_2$); $m/z$ 233 ($M^+ - NO_2$, 32), 195 (23), 133 (100). Anal. Calcd for $C_{15}H_{11}O_4N$: C, 66.91; H, 4.12; N, 5.20. Found: C, 66.80; H, 4.12; N, 5.20.

**3-(1-Nitroethyl)-7-methoxy-1(3*H*)-isobenzofuranone (29e).** The nitro lactone **29e**, prepared from 7-methoxyphthalaldehydic acid (**27b**) and nitroethane (**28b**), was isolated in 90% yield as an oil which solidified on standing. The only indication in the $^1H$ NMR spectrum that the material was a mixture were the two doublets at 5.86 and 5.98 ppm. The $^{13}C$ NMR spectrum clearly showed the presence of a 1:1 mixture of diastereoisomers: $^1H$ NMR ($CDCl_3$) $\delta$ 1.54 (t, 3 H, $J$ = 6.38 Hz, C*H*$_3$), 4.01 (s, 3 H, OC*H*$_3$), 4.60–5.12 (m, 1 H, C*H*$NO_2$), 5.86, 5.98 (d, 1 H combined, $J$ = 5.7 Hz, Ar C*H*), 6.90–7.16 (m, 2 H, Ar *H*), 7.56–7.80 (m, 1 H, Ar *H*); $^{13}C$ NMR ($CDCl_3$) $\delta$ 11.9, 14.1 (*C*$H_3$), 55.9, 78.2, 78.3, 83.1, 83.2, 112.1, 113.5, 114.4, 136.8, 137.2, 145.4, 147.4, 158.8, 166.6, 166.9 (*C*=O); IR (film, $cm^{-1}$) 2845 (Ar $OCH_3$), 1773 (C=O), 1555, 1362 ($NO_2$).

**3-[(4-Methoxyphenyl)nitromethyl]-7-methoxy-1(3*H*)-isobenzofuranone (29f).** The nitro lactone **29f**, prepared from 7-methoxyphthalaldehydic acid (**27b**) and (4-methoxyphenyl)-nitromethane (**28e**), was isolated in 45% yield as an oil which

solidified on standing. A $^1H$ NMR spectrum of the material indicated it was an 8:2 mixture of diastereoisomers: $^1H$ NMR ($CDCl_3$) (major isomer) $\delta$ 3.85 (s, 3 H, $OCH_3$), 3.95 (s, 3 H, $OCH_3$), 5.25 (d, 1 H, $J$ = 10.12 Hz, $CHNO_2$), 5.29 (d, 1 H, $J$ = 7.48 Hz, Ar $H$), 6.23 (d, 1 H, $J$ = 10.12 Hz, Ar $CH$), 6.8–7.2 (m, 3 H, Ar $H$), 7.2–7.7 (m, 3 H, Ar $H$); IR (KBr, $cm^{-1}$) 2843 (Ar OMe), 1772 (C=O), 1612, 1601, 1563, 1515, 1488 (Ar C=C).

**3-[(3,4-Dimethoxyphenyl)nitromethyl]-7-methoxy-1-(3*H*)-isobenzofuranone (29g).** The nitro lactone **29g**, prepared from 7-methoxyphthalaldehydic acid (**21b**) and (3,4-dimethoxyphenyl)nitromethane (**28f**), was isolated in 40% yield as an oil which solidified on standing. A $^1H$ NMR spectrum of the material indicated that it was an 8:2 mixture of diastereoisomers: $^1H$ NMR ($CDCl_3$) (major isomer) $\delta$ 3.89 (s, 3 H, $OCH_3$), 3.95 (s, 3 H, $OCH_3$), 3.98 (s, 3 H, $OCH_3$), 5.25 (d, 1 H, $J$ = 10.12 Hz, $CHNO_2$), 5.84 (d, 1 H, $J$ = 7.91 Hz, Ar $H$), 6.26 (d, 1 H, $J$ = 10.12 Hz, Ar $CH$), 6.8–7.6 (m, 5 H, Ar $H$); IR (KBr, $cm^{-1}$) 2843 (Ar OMe), 1773 (C=O), 1603, 1562, 1518, 1488, 1464 (Ar C=C).

**General Procedure for Preparation of (Nitroalkyl)benzoic Acids from (Nitroalkyl)Isobenzofuranones.**[16] The (nitroalkyl)isobenzofuranone **29** (4.6 mmol) was dissolved in DMSO (10 mL) and placed in a water bath (25 °C). Sodium borohydride (3.5 mmol) was added slowly in small portions to prevent excessive frothing, and the resulting mixture was stirred for 1 h at room temperature. The reaction was quenched by addition of acetic acid (0.9 mL), water (25 mL), and hydrochloric acid (12 N, 2.3 mL). The reaction was extracted with ethyl acetate (3 × 20 mL), and the combined ethyl acetate extracts were washed with water (3 × 15 mL) and brine, dried ($MgSO_4$), filtered, and evaporated. Chromatography of the residue on silica gel (20 g, $CH_2Cl_2$ and then EtOAc) yielded pure (nitroalkyl)benzoic acid **30**.

**2-(2-Nitroethyl)benzoic Acid (30a).** The acid **30a** was isolated in 93% yield as a pale yellow solid with mp 127–129 °C ($CH_2Cl_2$–hexanes): $^1H$ NMR ($CDCl_3$) $\delta$ 3.71 (t, 2 H, $J$ = 7.0 Hz, Ar $CH_2$), 4.74 (t, 2 H, $J$ = 7.0 Hz, $CHNO_2$), 7.20–7.80 (m, 3 H, Ar $H$), 8.17 (dd, 1 H, $J$ = 8 Hz, $J$ = 2 Hz, Ar $H$); IR (film, $cm^{-1}$) 3400–2400 ($CO_2H$), 1693 (C=O), 1554, 1379 ($NO_2$).

**2-(2-Nitropropyl)benzoic Acid (30b).** The acid **30b** was isolated in 77% yield as a white solid with mp 118–120 °C ($CH_2Cl_2$–hexanes): $^1H$ NMR ($CDCl_3$) $\delta$ 1.63 (d, 3 H, $J$ = 7.0 Hz, $CH_3$), 3.40–3.80 (m, 2 H, Ar $CH_2$), 4.70–5.18 (m, 1 H, $CHNO_2$), 7.10–7.60 (m, 3 H, Ar $H$), 8.16 (dd, 1 H, $J$ = 8 Hz, $J$ = 2 Hz, Ar $H$); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.5, 40.0, 84.7, 127.4, 127.8, 132.2, 132.4, 133.6, 138.9, 172.4 (C=O); IR (film, $cm^{-1}$) 3400–2400 ($CO_2H$), 1692 (C=O), 1550, 1362 ($NO_2$); $m/z$ (FAB) 210 ($M^+$ + 1, 11), 194 (100), 192 (16), 179 (47), 176 (42), 163 (31), 145 (27), 133 (77).

**2-(2-Nitrobutyl)benzoic Acid (30c).** Recrystallization ($CH_2Cl_2$–hexanes) yielded 0.77 g (70%) of **30c** as white crystals with mp 134–136 °C: $^1H$ NMR ($CDCl_3$) $\delta$ 1.03 (t, 3 H, $J$ = 7.3 Hz, $CH_2CH_3$), 1.70–2.30 (m, 2 H, $CH_2CH_3$), 3.36 (dd, 1 H, $J$ = 9.2 Hz, $J$ = 14.0 Hz, Ar $CH$), 3.76 (dd, 1 H, $J$ = 4.0 Hz, $J$ = 14.0 Hz, Ar $CH$), 4.64–5.00 (m, 1 H, $CHNO_2$), 7.12–7.64 (m, 3 H, Ar $H$), 8.17 (dd, 1 H, $J$ = 2.2 Hz, $J$ = 7.0 Hz, Ar $H$); $^{13}C$ NMR ($CDCl_3$) $\delta$ 10.2, 27.5, 38.6, 91.4, 127.4, 127.8, 132.2, 132.5, 133.8, 139.1, 172.8 (C=O); IR (film, $cm^{-1}$) 3400–2400 ($CO_2H$), 1691 (C=O), 1550, 1375 ($NO_2$); $m/z$ (FAB) 177 ($M^+ - NO_2$, 23), 176 (70), 159 (30), 158 (27), 147 (47), 135 (100), 131 (55). Anal. Calcd for $C_{11}H_{13}O_4N$: C, 59.19; H, 5.87; N, 6.28. Found: C, 59.28; H, 5.87; N, 6.19.

**2-(2-Phenyl-2-nitroethyl)benzoic Acid (30d).** Recrystallization of the crude product ($CH_2Cl_2$–hexanes) yielded 0.64 g (85%) of **30d** as white crystals with mp 150–153 °C: $^1H$ NMR ($CDCl_3$) $\delta$ 3.80–4.16 (m, 2 H, Ar $CH_2$), 5.84–6.04 (m, 1 H, $CHNO_2$), 7.12–7.60 (m, 8 H, Ar $H$), 8.18–8.24 (m, 1 H, Ar $H$); $^{13}C$ NMR ($CDCl_3$) $\delta$ 39.7, 92.3, 127.4, 127.7, 128.0, 129.1, 129.7, 132.6, 133.8, 134.9, 138.5, 172.3 (C=O); IR (KBr, $cm^{-1}$) 3400–2500 ($CO_2H$), 1689 (C=O), 1553, 1369 ($NO_2$); $m/z$ 235 ($M^+ - NO_2$, 48), 207 (100), 194 (14), 178 (39), 118 (100). Anal. Calcd for $C_{15}H_{13}O_4N$: C, 66.41; H, 4.83; N, 5.16. Found: C, 66.69; H, 5.01; N, 4.95.

**2-(2-Nitropropyl)-7-methoxybenzoic Acid (30e).** The acid **30e** was isolated in 95% yield as an oil: $^1H$ NMR ($CDCl_3$) $\delta$ 1.58 (d, 3 H, $J$ = 6.6 Hz, $CH_3$), 3.24–3.40 (m, 2 H, Ar $CH_2$), 3.92 (s, 3 H, $OCH_3$), 4.72–5.16 (m, 1 H, $CHNO_2$), 6.72–7.02 (m, 2 H, Ar $H$), 7.23–7.48 (m, 1 H, Ar $H$); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.1, 39.2, 56.3, 84.3, 110.8, 120.7, 123.4, 132.0, 136.9, 157.5, 170.2 (C=O); IR (KBr, $cm^{-1}$) 3500–2500 ($CO_2H$), 2842 (Ar $OCH_3$), 1731, 1701 (C=O), 1551, 1360 ($NO_2$).

**2-[2-(4-Methoxyphenyl)-2-nitroethyl]-7-methoxybenzoic Acid (30f).** A modified procedure was employed. Aqueous sodium hydroxide (1 N, 2 mL) was added to the reaction prior to the addition of sodium borohydride. The acid **30f** was isolated in 73% yield as a solid: $^1H$ NMR ($CDCl_3$) $\delta$ 3.78 (s, 3 H, $OCH_3$), 3.91 (s, 3 H, $OCH_3$), 3.4–4.0 (m, 2 H, Ar $CH_2$), 5.76–5.98 (m, 1 H, $CHNO_2$), 6.70–7.04 (m, 4 H, Ar $H$), 7.20–7.52 (m, 3 H, Ar $H$); $^{13}C$ NMR ($CDCl_3$) $\delta$ 39.0, 55.2, 56.4, 91.6, 110.9, 114.2, 120.8, 123.9, 126.8, 128.9, 132.1, 137.1, 157.6, 160.5, 169.9 (C=O).

**2-[2-(3,4-Dimethoxyphenyl)-2-nitroethyl]-7-methoxybenzoic Acid (30g).** A modified procedure was employed. Aqueous sodium hydroxide (1 N, 2 mL) was added to the reaction prior to the addition of sodium borohydride. The acid **30g** was isolated in 81% yield as a solid: $^1H$ NMR ($CDCl_3$) $\delta$ 3.86 (s, 3 H, $OCH_3$), 3.89 (s, 3 H, $OCH_3$), 3.93 (s, 3 H, $OCH_3$), 3.36–4.00 (m, 2 H, Ar $CH_2$), 5.76–6.00 (m, 1 H, $CHNO_2$), 6.72–7.16 (m, 5 H, Ar $H$), 7.20–7.48 (m, 1 H, Ar $H$); $^{13}C$ NMR ($CDCl_3$) $\delta$ 39.0, 55.9, 56.3, 91.8, 110.3, 110.9, 111.1, 120.3, 123.8, 127.0, 132.1, 136.9, 149.1, 150.0, 157.6, 170.0 (C=O).

**2-(2-Oxopropyl)benzoic Acid (31b).**[19] A solution of the nitro acid **30b** (971 mg, 4.65 mmol) and sodium methoxide (501 mg, 9.3 mmol) in methanol (20 mL) was added to a vigorously stirred solution of $TiCl_3$ (14.3 mL, 18.6 mmol, 20% in 6 N hydrochloric acid) and ammonium acetate (8.6 g, 111.5 mmol) in water (30 mL) at room temperature. The initial purple solution became a blue gray suspension. The reaction was stirred for 1.5 h, diluted with water (70 mL), and acidified with 12 M hydrochloric acid to pH 1. Sodium chloride (1 g) was added, and the mixture was extracted with ether (100 mL). The ether layer was washed with water (4 × 30 mL) and brine (30 mL), dried ($MgSO_4$), filtered, and evaporated at reduced pressure. Chromatography of the residue on silica gel (50 g, $CH_2Cl_2$ and then EtOAc) gave 593 mg (72%) of **31b** as a pale brown solid: $^1H$ NMR ($CDCl_3$) $\delta$ 2.16 (br s, 3 H, $COCH_3$), 3.96 (br s, 2 H, Ar $CH_2$), 7.1–7.7 (m, 3 H, Ar $H$), 8.0–8.2 (m, 1 H, Ar $H$); IR ($CDCl_3$, $cm^{-1}$) 3600–2400 ($CO_2H$), 1700 (C=O); $m/z$ (FAB) 179 ($M^+$ + 1, 87), 161 (100), 135 (29), 133 (18), 119 (40).

**General Procedure for Titanium Trichloride Conversion of (Nitroalkyl)benzoic Acids to Isobenzopyran-1-ones.** A solution of the (nitroalkyl)benzoic acid **30** (4.65 mmol) and sodium methoxide (9.3 mmol) in THF (6 mL) was added to a solution of $TiCl_3$ (18.6 mmol, 20% in aqueous 6 N HCl) and ammonium acetate (111.5 mmol) in water (20 mL) at room temperature under a nitrogen atmosphere. The reaction was stirred 1.0–1.5 h, at which time, the initial purple color faded. The solution was acidified with 12 N hydrochloric acid to pH 1 and extracted with ethyl acetate (2 × 75 mL). The combined ethyl acetate extracts were washed with water (2 × 40 mL) and brine (25 mL), and then dried ($MgSO_4$), filtered, and concentrated. The residue was dissolved in an ethyl acetate solution (10 mL) containing perchloric acid (0.01 M) and acetic anhydride (1 M). The reaction was stirred for 0.5–1.0 h at room temperature. Ether (30 mL) was added, and the solution was washed with aqueous sodium bicarbonate (3 × 20 mL), water (20 mL), and brine (10 mL), and then dried ($MgSO_4$), filtered, and evaporated under reduced pressure. Chromatography of the residue on silica gel (5–20 g, $CH_2Cl_2$) furnished pure **33**.

**2-Benzopyran-1(1*H*)-one (33a).** A modified procedure was employed. The perchloric acid solution was heated at reflux for 0.5 h. The benzopyranone **33a** was isolated in 20% yield as a pale yellow low-melting solid (lit.[24] mp 45–46 °C): $^1H$ NMR ($CDCl_3$) $\delta$ 6.49 (d, 1 H, $J$ = 5.7 Hz, vinyl $H$), 7.28 (d, 1 H, $J$ = 5.7 Hz, vinyl $H$), 7.2–8.0 (m, 3 H, Ar $H$), 8.31 (br d, 1 H, $J$ = 7.5 Hz, Ar $H$); IR (film, $cm^{-1}$) 1728 (C=O), 1638 (C=C); mass spectrum, $m/z$ 146 ($M^+$, 39), 118 (100), 97 (59).

**3-Methyl-2-benzopyran-1(1*H*)-one (33b).** The benzopyranone **33b** was isolated in 52% yield as a pale yellow solid with mp 66–69 °C (hexanes) (lit.[25] mp 71–72 °C); $^1H$ NMR ($CDCl_3$) $\delta$ 2.28 (s, 3 H, $CH_3$), 6.26 (s, 1 H, vinyl $H$), 7.2–7.8 (m, 3 H, Ar $H$), 8.24 (br d, 1 H, $J$ = 8.4 Hz, Ar $H$); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.4 ($CH_3$), 103.3, 119.7, 124.7, 127.3, 129.2, 134.5, 137.4, 154.3, 162.7 (C=O); IR ($CDCl_3$, $cm^{-1}$) 1728 (C=O), 1663 (C=C); $m/z$ 160 ($M^+$,

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100), 145 ($M^+ - CH_3$, 27), 134 (36), 118 (43), 105 (32). Anal. Calcd for $C_{10}H_8O_2$: C, 74.99; H, 5.03. Found: C, 74.75; H, 5.06.

**3-Ethyl-2-benzopyran-1(1*H*)-one (33c).** The benzopyranone **33c** was isolated in 43% yield as a pale yellow solid with mp 66–70 °C (benzene–hexanes) (lit.[26] mp 72–73 °C): $^1H$ NMR ($CDCl_3$) $\delta$ 1.27 (t, 3 H, $J$ = 7.5 Hz, $CH_2CH_3$), 2.56 (q, 2 H, $J$ = 7.5 Hz, $CH_2CH_3$), 6.24 (s, 1 H, vinyl *H*), 7.3–7.8 (m, 3 H, Ar *H*), 8.23 (br d, 1 H, $J$ = 8.4 Hz, Ar *H*); $^{13}C$ NMR ($CDCl_3$) $\delta$ 11.1 ($CH_2CH_3$), 26.6, 101.9, 120.1, 125.0, 127.4, 129.4, 134.6, 137.6, 159.4, 162.9 (*C*=O); IR ($CDCl_3$, $cm^{-1}$) 1724 (C=O), 1656 (C=C); $m/z$ 174 ($M^+$, 100), 159 (12), 145 (44), 118 (46), 105 (35). Anal. Calcd for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79. Found: C, 74.96; H, 5.89.

**3-Phenyl-2-benzopyran-1(1*H*)-one (33d).** The benzopyranone **33d** was isolated in 32% yield as a pale yellow solid with mp 84–85 °C (benzene–hexanes) (lit.[27] mp 91–92 °C): $^1H$ NMR ($CDCl_3$) $\delta$ 6.93 (s, 1 H, vinyl *H*), 7.3–8.0 (m, 8 H, Ar *H*), 8.2–8.4 (m, 1 H, Ar *H*); $^{13}C$ NMR ($CDCl_3$) $\delta$ 101.7, 120.5, 125.2, 125.9, 128.0, 128.7, 129.5, 129.9, 131.9, 134.8, 137.5, 153.6, 162.1 (*C*=O); IR ($CDCl_3$, $cm^{-1}$) 1729 (C=O), 1638 (C=C); $m/z$ 232 ($M^+$, 100), 194 (76), 165 (52), 105 (30). Anal. Calcd for $C_{15}H_{10}O_2$: C, 81.07; H, 4.54. Found: C, 80.92; H, 4.75.

**3-Methyl-7-methoxy-2-benzopyran-1(1*H*)-one (33e).** The benzopyranone **33e** was isolated in 27% yield as a pale yellow solid with mp 105–108 °C (benzene–hexanes): $^1H$ NMR ($CDCl_3$) $\delta$ 2.23 (s, 3 H, $CH_3$), 3.98 (s, 3 H, $OCH_3$), 6.14 (s, 1 H, vinyl *H*), 6.86–7.00 (m, 2 H, Ar *H*), 7.44–7.50 (m, 1 H, Ar *H*); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.1 ($CH_3$), 56.0 ($OCH_3$), 103.3, 109.2, 114.9, 116.8, 135.4, 136.9, 140.4, 154.7, 161.3 (*C*=O); IR ($CDCl_3$, $cm^{-1}$) 2842 (Ar OMe), 1728 (C=O), 1669 (C=C); $m/z$ 230 ($M^+$, 59), 175 (9), 161 (73). Anal. Calcd for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.18; H, 5.35.

**3-(4-Methoxyphenyl)-7-methoxy-2-benzopyran-1(1*H*)-one (33f).** The benzopyranone **33f** was isolated in 27% yield as a pale yellow solid with mp 143–146 °C (benzene–hexanes): $^1H$ NMR ($CDCl_3$) $\delta$ 3.82 (s, 3 H, $OCH_3$), 3.97 (s, 3 H, $OCH_3$), 6.68 (s, 1 H, vinyl *H*), 6.70–7.04 (m, 4 H, Ar *H*), 7.40–7.84 (m, 3 H, Ar *H*); $^{13}C$ NMR ($CDCl_3$) $\delta$ 55.4, 56.3, 100.2, 109.4, 113.9, 114.2, 117.8, 124.5, 126.9, 135.7, 140.9, 154.0, 161.1, 161.7 (*C*=O); $m/z$ 282 ($M^+$, 100), 254 (74), 239 (23), 211 (23). Anal. Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.23. Found: C, 71.91; H, 5.14.

**General Procedure for Nef Conversion of (Nitroalkyl)benzoic Acids to Isobenzopyran-1-ones.**[23] A solution of the (nitroalkyl)benzoic acid **30** (972 mg, 3.60 mmol) in aqueous sodium hydroxide (1 N, 15 mL) and methanol (2 mL) was added dropwise to a chilled (0 °C) solution of sulfuric acid (9 mL, concentrated) in methanol (36 mL). The resultant sky-blue colored solution was allowed to warm to room temperature, and the reaction mixture was stirred until the solution became colorless (1–2 h). Ethyl acetate (100 mL) and brine (50 mL) were added, and the layers were separated. The organic layer was washed with brine (3 × 50 mL) and transferred to a reaction flask. Perchloric acid (2 mL, 1 N in EtOAc) and acetic anhydride (11 mL) were added, and the solution was refluxed for 0.5–1 h. The reaction mixture was cooled to room temperature, and aqueous sodium bicarbonate (50 mL) was added cautiously to the stirring mixture. The reaction was continued for 0.5 h. The layers were separated, and the organic phase was washed successively with aqueous bicarbonate (50 mL), water (50 mL), and brine (40 mL), and then dried ($MgSO_4$), filtered, and evaporated at reduced pressure. Chromatography of the residue on silica gel (20 g, $CH_2Cl_2$) furnished the pure benzopyran-1-one **33**.

**3-Methyl-2-benzopyran-1(1*H*)-one (33b).** The benzopyranone **33b** was isolated in 84% yield and had physical and spectral properties identical with those of the compound prepared by method A.

**3-Ethyl-2-benzopyran-1(1*H*)-one (33c).** The benzopyranone **33c** was isolated in 85% yield and had physical and spectral properties identical with those of the material prepared by method A.

**3-Phenyl-2-benzopyran-1(1*H*)-one (33d).** The benzopyranone **33d** was isolated in 84% yield and had physical and spectral properties identical with those of the material prepared by method A.

**3-(4-Methoxyphenyl)-7-methoxy-2-benzopyran-1(1*H*)-one (33f).** The benzopyranone **33f** was isolated in 79% yield and had physical and spectral properties identical with those of the material prepared by method A.

**Abbreviated Procedure to Isobenzofuranones from (Nitroalkyl)isobenzofuranones.** Sodium borohydride (0.55 g, 15 mmol) was added in small portions to a solution of nitro lactone **29** (4.03 g, 18.2 mmol) dissolved in dimethyl sulfoxide (40 mL) at 10 °C and stirred at room temperature for 1.5 h. Aqueous sodium hydroxide (1 N, 55 mL) was added. The basic solution was added dropwise to a chilled (0 °C) solution of concentrated sulfuric acid (29 mL) in methanol (115 mL). The reaction mixture was stirred at room temperature until the blue colored solution became colorless (1.5 h). Ethyl acetate (500 mL) was added, and the layers were separated. The ethyl acetate solution was washed with brine (4 × 50 mL). The first brine wash was back-extracted with ethyl acetate (100 mL), which was then washed with brine (2 × 40 mL) again. The combined organic solutions were transferred to a reaction flask. Perchloric acid (5 mL, 1 N in EtOAc) and acetic anhydride (20 mL) were added, and the reaction mixture was heated at reflux for 1 h. The solution was cooled to room temperature, and aqueous and solid sodium bicarbonate were added until $CO_2$ evolution ceased. The layers were separated, and the organic phase was washed with aqueous bicarbonate (2 × 100 mL), water (70 mL), and brine (50 mL), and then dried ($MgSO_4$), filtered, and evaporated at reduced pressure. Chromatography of the residue on silica gel (50 g, $CH_2Cl_2$) yielded pure isobenzopyran-1-one **33**.

**3-Methyl-2-benzopyran-1(1*H*)-one (33b).** The benzopyranone **33b** was isolated in 64% yield and had physical and spectral properties identical with those of the material that was prepared by method A.

**3-Ethyl-2-benzopyran-1(1*H*)-one (33c).** The benzopyranone **33c** was isolated in 85% yield and had physical and spectral properties identical with those of the material that was prepared by method A.

**3-Methyl-7-methoxy-2-benzopyran-1(1*H*)-one (33e).** The benzpyranone **33e** was isolated in 65% yield and had physical and spectral properties identical with those of the material that was prepared by method A.

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**Registry No.** **27a**, 16859-59-9; **27b**, 73713-38-9; **28a**, 75-52-5; **28b**, 79-24-3; **28c**, 108-03-2; **28d**, 622-42-4; **28e**, 29559-26-0; **28f**, 114131-33-8; **29a**, 3598-68-3; (R*,R*)-**29b**, 97049-75-7; (R*,S*)-**29b**, 97049-60-0; **29c**, 79017-07-5; (R*,R*)-**29c**, 115912-82-8; (R*,S*)-**29c**, 115912-83-9; (R*,R*)-**29d**, 115912-84-0; (R*,S*)-**29d**, 115912-85-1; (R*,R*)-**29e**, 115912-86-2; (R*,S*)-**29e**, 115912-87-3; (R*,R*)-**29f**, 115912-88-4; (R*,S*)-**29f**, 115912-89-5; (R*,R*)-**29g**, 115912-90-8; (R*,S*)-**29g**, 115912-91-9; **30a**, 115912-92-0; **30b**, 115912-93-1; **30c**, 115912-94-2; **30d**, 115912-95-3; **30e**, 115912-96-4; **30f**, 115912-97-5; **30g**, 115912-98-6; **31b**, 2852-91-7; **32a**, 115912-99-7; **32b**, 115913-00-3; **33a**, 491-31-6; **33b**, 29539-21-7; **33c**, 26477-57-6; **33d**, 4809-08-9; **33e**, 830-54-6; **33f**, 36640-12-7.

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