risen to above 60 °C with the formation of a bright yellow precipitate. Filtration and washing with water gave crude enol aldehyde **20** (1.4 g, 45%): mp 97–102 °C; IR ($CHBr_3$) 1625, 1580, 1225, 1205, 985 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 10.50 (d, 1 H, J = 2 Hz), 10.18 (m, 1 H), 8.67–7.40 (m, 3 H), 3.33 (s, 2 H); ^{13}C NMR (MeOH) 194.0 (d), 189.0 (d), 181.5 (d), 154.9 (s), 146.6 (d), 125.1 (s), 117.3 (s), 111.1 (s), 24.4 (t) ppm. Anal. Calcd for $C_9H_7ClO_3$: C, 54.43; H, 3.55. Found: C, 54.33; H, 3.40.

Attempts to purify enol aldehyde **20** led to decomposition; vacuum sublimation afforded trialdehyde **21** in 39% yield as reported elsewhere.[13] However, solutions of **20** in aqueous potassium carbonate were stable at 20 °C for several weeks.

4-Chloro-3-(4-morpholinylmethyl)phenol (29). To a solution of *N*-formylmorpholine (13.7 g, 0.119 mol) in trichloroethylene (20 mL) was added phosphorus oxychloride (14 g, 91.3 mmol). The mixture was stirred for 10 min at 20 °C, placed in an ice–water bath, and cyclohexane-1,4-dione (3.36 g, 30 mmol) then added; the temperature of the very exothermic reaction was kept below 50 °C. After 72 h, the mixture was poured into dichloromethane (50 mL) and water (50 mL); solid sodium carbonate was added with constant stirring until the aqueous layer was neutral. The organic layer was dried and evaporated to give an oil, which on trituration with 1:9 chloroform:trichloroethylene afforded phenol **29** (1.26 g, 16%) that crystallized from isopropyl alcohol as prisms: mp 133–134 °C; IR ($CHBr_3$) 3400 (bd), 1560, 1465, 1440, 905, 870, 855, 810 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 9.73 (s, 1 H, OH), 7.30 (d, 1 H, J = 9 Hz), 7.05 (d, 1 H, J = 3 Hz), 6.80 (dd, 1 H, J = 3 and 9 Hz), 3.80–3.30 (m, 6 H), 2.60–2.30 (m, 4 H). Anal. Calcd for $C_{11}H_{14}ClNO_2$: C, 58.02; H, 6.20; N, 6.15. Found: C, 58.01; H, 6.31; N, 5.93.

1-(2-(*N*,*N*-Dimethylamino)-1-formylvinylene)-3,4-dihydronaphthalene-2-carboxaldehyde (44). Phosphorus oxychloride (10.5 g, 68.5 mmol) was added over 2 min with stirring to DMF (10 g, 0.137 mmol) at 5 °C. Addition of 3,4-dihydro-1-methylnaphthalene[14] (3.0 g, 20.8 mmol) gave a mixture that was heated at 80 °C for 14 h. The dark solution was poured into 10% aqueous sodium acetate (150 mL) and the mixture extracted with dichloromethane (2 × 50 mL). The organic layers were combined, washed first with 5% aqueous sodium acetate and then with water, dried, and evaporated to afford a residue that was triturated with 60–80 °C petroleum (2 × 30 mL). The gum remaining was dissolved in chloroform (1 mL) and eluted through silica gel (30 g) by using consecutively as eluents ethyl acetate, chloroform, and dichloromethane. All the eluents were combined and evaporated to give an oil (1.4 g), which on trituration with 60–80 °C petroleum (10 mL) gave aldehyde **44** (0.94 g, 18%) that crystallized from ethyl acetate as yellow needles: mp 133–134 °C; IR ($CHBr_3$) 2950, 2890, 2840, 1640, 1600 (vs, broad), 1560, 905, 855, 750 cm^{-1}); ^1H NMR ($CDCl_3$) δ 9.70 (s, 1 H), 9.10 (s, 2 H), 7.20 (s, 4 H), 2.80 (s, 7 H). Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.30; H, 6.80;, N, 5.46.

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Registry No. **1**, 123-54-6; **3**, 874-42-0; **5**, 108009-48-9; **7**, 108009-49-0; **8a**, 101392-95-4; **9**, 930-68-7; **10**, 5682-75-7; **11**, 56671-81-9; **20**, 108009-50-3; **26**, 637-88-7; **29**, 108009-51-4; **40**, 4373-13-1; **44**, 108009-52-5; DMF, 68-12-2; $POCl_3$, 10025-87-3; *N*-formylmorpholine, 4394-85-8; cyclohexane-1,3-dione, 504-02-9; *N*-formylpyrrolidine, 3760-54-1; 2-bromocyclohexane-1,3-dione, 60060-44-8.

(13) Katritzky, A. R.; Marson, C. M.; Wang, Z., in press.

(14) Garbisch, E. W. *J. Org. Chem.* **1961**, *26*, 4165.

Reactions of Alkyl-Substituted 2-Cyclohexen-1-ones with Vilsmeier Reagents

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Various 2-cyclohexen-1-ones underwent formylation on treatment with formamides and $POCl_3$ at 20 °C. Two distinct reactivity patterns were found: type A, in which mono-, di-, or triformylated olefins or benzenes are formed, and type B, in which a 3-methyl-2-cyclohexen-1-one undergoes formylation at the carbon atom of the 3-substituent. Several 2-cyclohexen-1-ones afford formylated products analogous to those obtained from the reaction of 3-oxo-4-ene steroids with Vilsmeier reagents. Mechanistic rationales for several Vilsmeier reactions are proposed.

Whereas β-chlorovinyl aldehydes are the normal products from the reaction of cyclohexanones with Vilsmeier reagents,[1] cyclohexane-1,3-diones can give rise to a variety of formylated products.[2,3] Cyclohexane-1,3-diones exist predominantly in solution at 20 °C in a monoenol form which contains both olefinic and ketonic moieties. Alicyclic olefins can themselves form more than one product under Vilsmeier conditions (e.g.,[4] **2** → **1** and **3**), whereas 3-oxo-4-ene steroids **5** can give monoformylated structures (e.g., **4**,[5] **8b**,[6] and **8c**[6]), diformyl benzenoid derivatives (e.g., **6**[5]), or simply chloroolefins (e.g., **8a**[6]). We classify these reaction pathways as types A1, A2, and B (Scheme I).

We now report a systematic study of the reaction of alkyl-substituted 2-cyclohexen-1-ones with Vilsmeier reagents. Our aims were to extend the scope of such formylation reactions and to provide some rationale for the products of those reactions, whether reported here or previously.

Reaction of 4-isopropyl-2-cyclohexen-1-one with a 1.3:1 molar ratio of *N*-formylmorpholine/$POCl_3$ in trichloro-

(1) Pulst, M.; Weissenfels, M. *Z. Chem.* **1976**, *16*, 337.
(2) Katritzky, A. R.; Marson, C. M. *Tetrahedron Lett.* **1985**, *26*, 4715.
(3) Pulst, M.; Hollborn, B.; Weissenfels, M. *J. Prakt. Chem.* **1979**, *321*, 671.
(4) Grimwade, M. J.; Lester, M. G. *Tetrahedron* **1969**, *25*, 4535.
(5) Laurent, H.; Wiechert, R. *Chem. Ber.* **1968**, *101*, 2393.
(6) Sciaky, R.; Mancini, F. *Tetrahedron Lett.* **1965**, *2*, 137.

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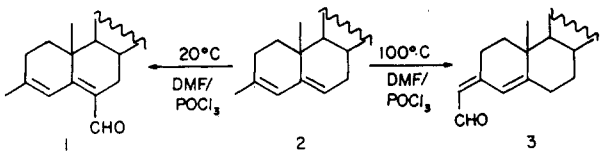
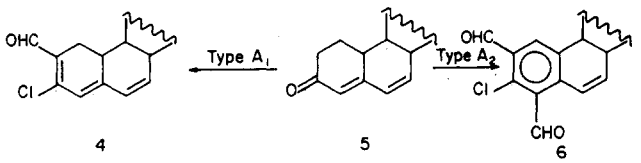
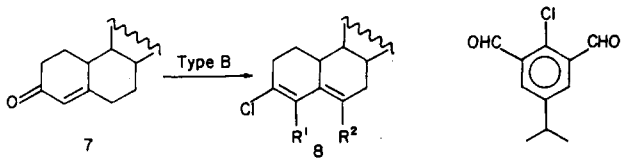
Scheme I

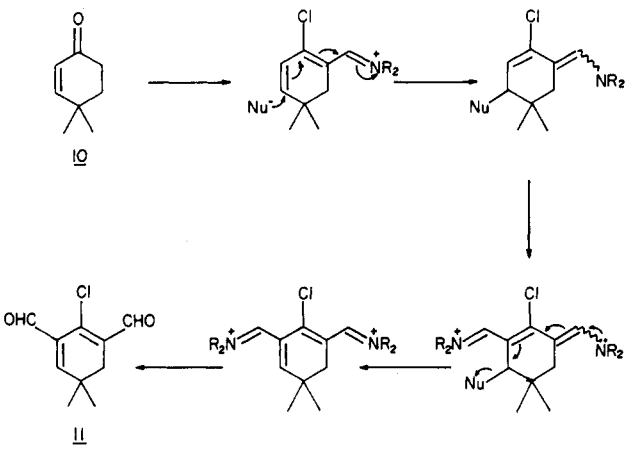






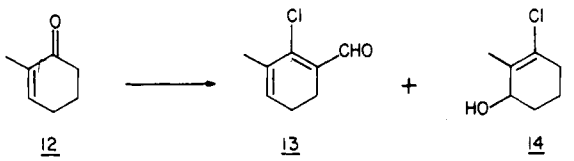
a $R^1 = R^2 = H$
b $R^1 = CHO$, $R^2 = H$
c $R^1 = H$, $R^2 = CHO$

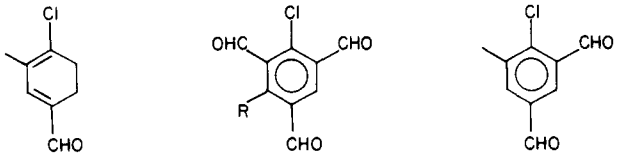
Scheme II



ethylene at 25 °C afforded the aromatic dialdehyde **9** (31%) as the sole isolated product. Under similar conditions, 4,4-dimethyl-2-cyclohexen-1-one (**10**) afforded the novel dialdehyde **11** (29%) as the only isolated product; NOE experiments clearly established the order of four substituents: olefinic hydrogen adjacent to the *gem*-dimethyl group, in turn adjacent to the methylene group, in turn adjacent to one of the formyl groups. Nucleophilic attack as shown in Scheme II is a plausible explanation for the formation of dialdehyde **11**.

Reaction of 2-methyl-2-cyclohexen-1-one (**12**) with a 1.3:1 molar ratio of *N*-formylmorpholine/$POCl_3$ in trichloroethylene at 25 °C and elution of the oil from the hydrolyzed reaction mixture with 40–60 °C petroleum ether afforded first the oily cyclohexadienal **13** (21%) and then a crystalline alcohol **14** (33%). Structure **13** was confirmed (and structure **15** excluded) by a substantial NOE observed for the olefinic hydrogen and one of the methylene groups. Formylation of ketone **12** had thus occurred at the 6-position, with none of the 4-formylated





a R = H
b R = Me
c R = OEt

derivative **15** being detected.

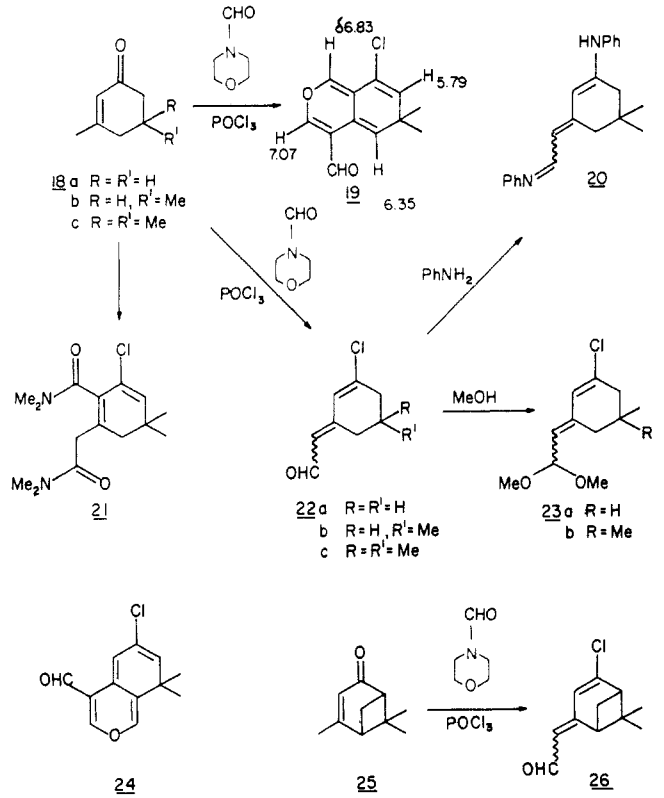
The reaction of 2-cyclohexen-1-one with *N*-formylmorpholine/$POCl_3$ at 20 °C gave an enol,[7] which soon underwent aerial oxidation to the trialdehyde **16a**. When 3-ethoxy-2-cyclohexen-1-one was reacted with a 1.3:1 molar ratio of *N*-formylmorpholine/$POCl_3$ in trichloroethylene at 25 °C, the phenetole **16c** was obtained in 31% yield as the sole isolated product. Similar formylations of methoxycyclohexadienes with oxidative aromatization have been reported by Raju and Rao:[8] 1-methoxy-1,4-cyclohexadiene, with DMF/$POCl_3$, afforded aldehyde **16a**. However, whereas these workers obtained[8] dialdehyde **17** from 1-methoxy-2-methyl-1,4-cyclohexadiene and DMF/$POCl_3$, no such product was formed from 2-methyl-2-cyclohexen-1-one (**12**) under our conditions. Evidently, acid-catalyzed hydrolysis of 1-methoxy-2-methyl-1,4-cyclohexadiene to ketone **12** is not the pathway by which dialdehyde **17** is formed.

In agreement with previous work,[9,10] the action of Vilsmeier reagents on 3,5-dimethyl-2-cyclohexen-1-one (**18b**) and 3,5,5-trimethyl-2-cyclohexen-1-one (isophorone) (**18c**) gave the cyclohexylideneacetaldehydes **22b** (73%) and **22c** (87%), respectively (both as *E*/*Z* mixtures; Scheme III). As previously reported,[10] along with aldehyde **22c** we obtained the pyran **19** (27%) as yellow prisms; the alternative structure **24** (not previously[10] considered) was ruled out on the basis of multiplicity and NOE studies on the ^1H NMR. The singlet at δ 7.07 gave a 19% NOE to the aldehydic signal; the multiplet at δ 6.83 gave no NOE. Significantly, irradiation of *either* the triplet (J = 1.5 Hz) at δ 6.35 *or* the doublet (J = 1.8 Hz) at δ 5.79 in each case gave a 22% NOE to the signal at δ 1.17. Interestingly, Janousek[11] reported that a dichloro methylene iminium salt reacted with isophorone (**18c**) to give diamide **21**; the mechanism of its formation is presumably similar to that of pyran **19**.

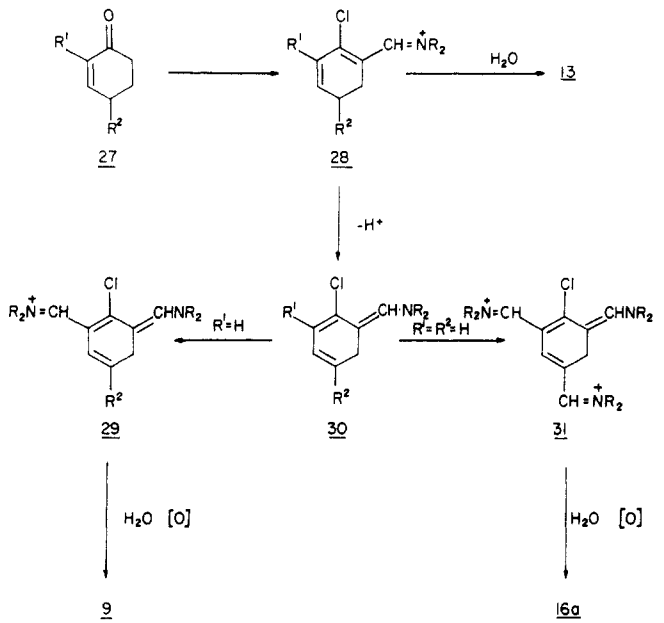
Reaction of 3-methyl-2-cyclohexen-1-one (**18a**) with a 1.3:1 molar ratio of *N*-formylmorpholine/$POCl_3$ in trichloroethylene at 25 °C gave a 66% yield of the unstable aldehyde **22a**; a similar reaction with (1*S*)-(−)-verbenone (**25**) afforded the aldehyde **26** in 95% yield. The cyclo-

(7) Katritzky, A. R.; Marson, C. M. *J. Org. Chem.*, preceding paper in this issue.
(8) Raju, B.; Krishna Rao, G. S. *Synthesis* **1985**, 779.
(9) Hoffman, W.; Mueller, E. *Ger. Offen. 2 152 193*, 1973; *Chem. Abstr.* **1973**, *79*, 18212.
(10) Traas, P. C.; Boelens, H.; Takken, H. J. *Recl. Trav. Chim. Pays-Bas.* **1976**, *95*, 308.
(11) Janousek, Z. Dissertation, University of Louvain, 1972.

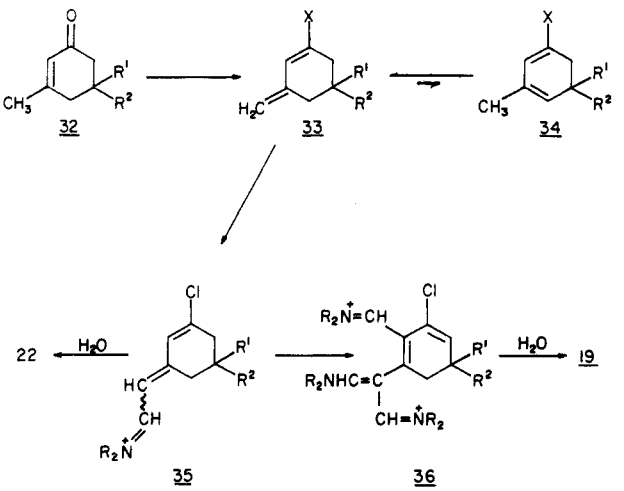
Scheme III



Scheme IV. Mechanism of Type A Reactions

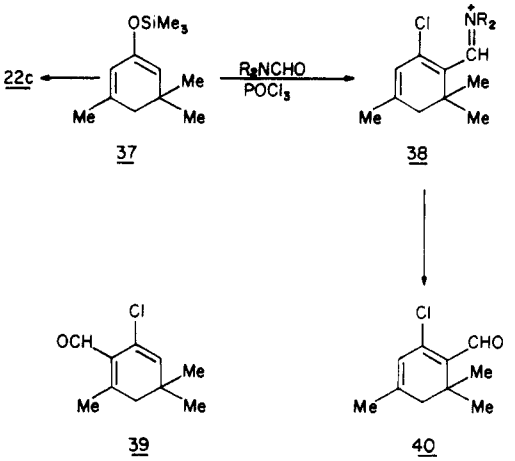


Scheme V. Mechanism of Type B Reactions



With 3-methyl-2-cyclohexen-1-ones **32** (Scheme V), type B reactions via the formation of cation **35** are favored. Although it is currently uncertain whether X is Cl or an oxygenated moiety (structures **33** and **34**), several exocyclic olefins analogous to **33** are known[12] to be favored thermodynamically over their endocyclic isomers (cf. diene **34**). Iminoalkylation of olefin **33** at the terminal position affords cation **35**, which can either undergo hydrolysis to aldehydes **22** or undergo further iminoalkylation ($R^4 = R^5 = Me$), giving cation **36** and hence, by hydrolysis, pyran **19**. Interestingly, 1-methoxy-5-methyl-1,4-cyclohexadiene reacts[8] with $DMF/POCl_3$ in a type A_2 reaction, affording trialdehyde **16b**; evidently, acid-catalyzed conversion of the above diene into 3-methyl-2-cyclohexen-1-one is not the route by which trialdehyde **16b** is formed.

Finally, we investigated the extent to which an enol ether (compared to the ketone) would control the course of the formylation. Reaction of the silyl ether **37** with a 1.3:1



molar ratio of *N*-formylmorpholine/$POCl_3$ in trichloroethylene at 25 °C gave aldehyde **22c** (87%) together with a new aldehyde, assigned the structure **40** (8%). The ^1H NMR at 300 MHz showed the signal for the olefinic hydrogen atom at δ 5.76 to be a symmetrical sextet (J = 1.8 Hz), clearly ruling out structure **39**. Aldehyde **40** is presumably produced via intermediate **38**.

hexylideneacetaldehydes (**22b** and **22c**) were further characterized as their DNP derivatives and as the acetals **23a** and **23b**. Reaction of aldehyde **22c** with 2 mol of aniline afforded the dark purple imine **20** in 81% yield.

The differences shown in the reactivity of 2-cyclohexen-1-ones with and without 3-methyl groups can be understood in terms of the pathways of Schemes IV and V. For ketone **27** (type A reaction; Scheme IV) iminoalkylation gives cation **28** (which leads by hydrolysis to product **13**). Deprotonation of cation **28** gives enamine **30**, which by a single further iminoalkylation gives **29** and hence products such as dialdehyde **9**. *Two* further iminoalkylations of enamine **30** lead, via cation **31**, to product **16a**.

Conclusions

The patterns of formylation previously reported for 3-oxo-4-ene steroids (types A_1, A_2, and B; Scheme I) are also observed in the formylation of several 2-cyclohexen-

(12) Taskinen, E.; Nummelin, K. *J. Org. Chem.* **1985**, *50*, 4844.

1-ones. Whereas formylation at the 4-position of a 2-cyclohexen-1-one is commonplace in a type A_2 pathway (involving aromatization), such formylation has not been observed when a type B pathway is followed. The mechanistic pathways for Vilsmeier formylations outlined here offer rationalization for the products reported here and many of those reported elsewhere.

Experimental Section

Melting points were determined on a Hoover Uni-melt capillary apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 297 spectrophotometer. ^1H NMR spectra were recorded with a Varian EM 360L spectrometer, and ^{13}C NMR spectra were recorded on a JEOL FX-100 spectrometer. "Evaporation" refers to removal of solvent under reduced pressure.

Starting Materials. (3-Chloro-5,5-dimethyl-2-cyclohexenylidene)acetaldehyde (**22c**) and 8-chloro-6,6-dimethyl-6*H*-2-benzopyran-4-carboxaldehyde (**19**) were prepared by the method of Traas, Boelens, and Takken.[10] 4,6,6-Trimethyl-2-((trimethylsilyl)oxy)cyclohexa-1,3-diene (**37**) was prepared by the method of Rubottom.[13]

1,3-Diformyl-2-chloro-5-isopropylbenzene (9). To a stirred mixture of *N*-formylmorpholine (6.9 g, 60 mmol) and trichloroethylene (10 mL) was added phosphorus oxychloride (7.0 g, 45.8 mmol) over 5 min at 5 °C. After stirring the resultant solution for 10 min at 20 °C, 4-isopropyl-2-cyclohexen-1-one (1.52 g, 11 mmol) was added dropwise at 15–20 °C. The mixture was then stirred at room temperature for 2 days. Methylene chloride (25 mL) was added, and the reaction mixture was brought to pH 7 with a solution of sodium carbonate (12.5 g, 0.118 mol) in water (75 mL). The aqueous layer was extracted with methylene chloride (3 × 50 mL). The combined organic layers were washed with water (60 mL) and dried over magnesium sulfate (10 g). Evaporating the solvent and keeping the residue at 0 °C overnight afforded the crude product, mp 110–112 °C. Recrystallization from aqueous ethanol gave **9** as prisms (0.70 g, 30%): mp 111–112 °C; IR (Bromoform) λ_{max} 2960, 2920 (w), 2870 (w), 1685 (C=O), 1570, 1380, 1325, 940 cm^{-1}; ^1H NMR ($CDCl_3$) 10.75 (s, 2 H, CHO), 8.15 (s, 2 H, Ar-H), 3.03 (m, 1 H, CH), 1.30 (d, 6 H, J = 7 Hz, $(CH_3)_2$); MS, m/z (rel intensity) 210 (M^+, 55), 195 (97), 181 (9). Anal. Calcd for $C_{11}H_{11}ClO_2$: C, 62.72; H, 5.26; Cl, 16.83. Found: C, 62.82; H, 5.31; Cl, 16.96.

1,3-Diformyl-2-chloro-5,5-dimethylcyclohexa-1,3-diene (11). To a stirred mixture of *N*-formylmorpholine (6.9 g, 60 mmol) and trichloroethylene (10 mL) at 5 °C was added phosphorus oxychloride (7 g, 45.8 mmol) over 5 min, at 5 °C. After stirring the resultant solution for 10 min at 20 °C, 4,4-dimethyl-2-cyclohexen-1-one (1.49 g, 12 mmol) was added dropwise. The mixture was then stirred at room temperature for 3 days. Methylene chloride (25 mL) was added, and the reaction mixture was brought to pH 7 with a solution of sodium carbonate (12.5 g, 0.118 mol) in water (75 mL). The aqueous layer was extracted with methylene chloride (3 × 50 mL). The combined organic layers were washed with water (60 mL) and dried with magnesium sulfate (10 g). The solvent was evaporated and the residue kept at 0 °C for 2 weeks; the crystals were washed with diethyl ether and sublimed in vacuo to give **11** as yellow prisms (0.70 g, 29%): mp 182–184 °C; IR ($CHBr_3$) 2950, 1650, 1605, 1190, 915 cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.53 (s, 1 H, CHO), 10.08 (s, 1 H, CHO), 7.18 (s, 1 H, CH), 2.48 (s, 2 H, CH_2), 1.15 (s, 6 H, CH_3); MS, m/z (rel intensity) 198 (M^+, 27), 183 (53), 169 (23); HRMS, calcd for $C_{10}H_{11}ClO_2$ 198.0447, found 198.0441.

Reaction of 2-Methyl-2-cyclohexen-1-one with *N*-Formylmorpholine and Phosphorus Oxychloride. To a stirred mixture of *N*-formylmorpholine (13.8 g, 0.117 mol) and trichloroethylene (20 mL) at 5 °C was added phosphorus oxychloride (13.8 g, 90 mmol) over 5 min, at 5 °C. After stirring the resultant solution for 10 min at 20 °C, 2-methyl-2-cyclohexen-1-one (3.0 g, 27 mmol) was added dropwise. The mixture was then stirred at room temperature for 2 h. Methylene chloride (50 mL) was added and the reaction mixture brought to pH 7 with a solution of sodium carbonate (25 g, 0.236 mmol) in water (150 mL). The aqueous layer was extracted with methylene chloride (3 × 100 mL); the combined organic layers were washed with water (120 mL) and dried over magnesium sulfate (20 g). Evaporation of the solvent under reduced pressure and purification of the residue by column chromatography on silica gel (80 g) using methylene chloride as eluent afforded first **13** as a yellow oil (0.91 g, 21%) and second **14** as needles (1.32 g, 33%): mp 74–76 °C. For **13**: IR (neat) 2940, 2850, 1650 (C=O; vs), 1540 (vs), 1430, 1370, 1210 (vs), 1055, 1015, 985, 795 cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.36 (s, 1 H, CHO), 6.23 (m, 1 H, CH), 2.40–2.33 (d, 4 H, $2CH_2$), 1.93 (s, 3 H, CH_3); MS, m/z (rel intensity) 156 (52), 121 (59). Calcd for C_8H_9ClO 156.0342. Found: 156.0341.

For **14**: IR (Bromoform) 3580 (OH), 3380 (broad; OH), 2940 (s), 1660, 1435, 1330, 1060, 950 (s), 900, 870, 840, 805 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.13 (br s, 1 H, CH), 2.33 (br s, 2 H), 1.90–1.50 (m, 8 H); MS, m/z (rel intensity) 144 (6), 128 (8), 111 (100), 93 (28). Anal. Calcd for $C_7H_{11}ClO$: C, 57.33; H, 7.50; Cl, 24.23. Found: C, 57.44; H, 7.57; Cl, 24.27.

The 2,4-dinitrophenylhydrazone of **13** was obtained as purple needles (81%) from ethyl acetate: mp 185–187 °C; MS, m/z (rel intensity) 336 (M^+, 27), 301 (96); HRMS, calcd for $C_{14}H_{13}ClN_4O_4$ 336.0625, found 336.0590.

Reaction of 2-Cyclohexen-1-one with *N*-Formylmorpholine and Phosphorus Oxychloride. To a stirred mixture of *N*-formylmorpholine (6.9 g, 60 mmol) and trichloroethylene (10 mL) at 5 °C was added phosphorus oxychloride (7 g, 45.8 mmol) over 5 min, at 5 °C. After stirring the resultant solution for 10 min at 20 °C, 2-cyclohexen-1-one (1.5 g, 15.6 mmol) was added dropwise. The mixture was then stirred at 20 °C for 3 days. The resultant tar was treated with water (10 mL); the temperature rose to 60 °C, the color of the mixture rapidly changing from black to yellow. More water (10 mL) was then added, and the yellow solid was filtered off, washed with water, and dried at 50 °C under reduced pressure. Vacuum sublimation and recrystallization from diisopropyl ether–ethyl acetate (9:1 v/v) gave **16a** as yellow prisms (1.2 g, 39%): mp 126.5–128.5 °C (lit.[8] mp 121–123 °C); IR (Bromoform) 2870 (w), 1680 (vs), 1570, 1210, 1045, 980, 930 cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.82 (s, 2 H, CHO), 10.32 (s, 1 H, CHO), 8.78 (s, 2 H, Ar-H). Anal. Calcd for $C_9H_5ClO_3$: C, 54.99; H, 2.56; Cl, 18.03. Found: C, 54.89; H, 2.64; Cl, 18.13.

1,3,5-Triformyl-2-chloro-6-ethoxybenzene (16c). To a stirred mixture of *N*-formylmorpholine (13.8 g, 0.117 mol) and trichloroethylene (20 mL) at 5 °C was added phosphorus oxychloride (13.8 g, 90 mmol) over 5 min. After stirring the resultant solution for 10 min at 20 °C, 3-ethoxy-2-cyclohexen-1-one (3.0 g, 21 mmol) was added dropwise so as to maintain the temperature below 20 °C. The mixture was then stirred at 20 °C for 3 days. Methylene chloride (50 mL) was added, and the reaction mixture was brought to pH 7 with a solution of sodium carbonate (25 g, 0.24 mol) in water (150 mL). The aqueous layer was extracted with methylene chloride (3 × 100 mL). The combined organic layers were extracted with water (120 mL) and dried over magnesium sulfate (20 g). Evaporation of the solvent and purification of the residue by column chromatography on silica gel using benzene–ethyl acetate (3:1) as eluent afforded **16c** as yellow prisms (1.6 g, 31%): mp 65–67 °C (from petroleum ether); IR (Bromoform) 2840, 1690 (C=O), 1580 (s), 1430, 1370, 1020, 950 cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.70 (s, 2 H, 2CHO), 10.50 (s, 1 H, CHO), 8.70 (s, 1 H, Ar-H), 4.30 (q, 2 H, J = 7 Hz, CH_2), 1.50 (t, 3 H, J = 7 Hz, CH_3); MS, m/z (rel intensity) 196 (M^+, 93), 195 (100), 167 (24), 132 (14). Anal. Calcd for $C_{11}H_9ClO_4$: C, 54.89; H, 3.74. Found: C, 54.83; H, 3.71.

(*E*)- and (*Z*)-(3-Chloro-2-cyclohexenylidene)acetaldehyde (22a). To a stirred mixture of *N*-formylmorpholine (13.8 g, 0.117 mol) and trichloroethylene (20 mL) at 5 °C was added phosphorus oxychloride (13.8 g, 90 mmol) over 5 min. After stirring the resultant solution for 10 min at 20 °C, 3-methyl-2-cyclohexen-1-one (3.0 g, 27 mmol) was added dropwise. The mixture was then stirred at 20 °C for 3 days. Methylene chloride (50 mL) was added and the reaction mixture brought to pH 7 with a solution of sodium carbonate (25 g, 0.236 mmol) in water (150 mL). The aqueous layer was extracted with methylene chloride (3 × 100 mL); the combined organic layers were washed with water (120 mL) and dried over magnesium sulfate (20 g). Evaporation of the solvent and purification of the residue by column chroma-

(13) Rubottom, G. M.; Gruber, J. M.; Juve, H. D.; Charleson, D. A. *Org. Synth.* **1986**, *64*, 118.

tography on silica gel using chloroform as eluent afforded a 3:2 E/Z isomeric mixture of **22a** as a yellow oil (2.8 g, 65%): IR (Bromoform) 2940, 2860, 1700, 1660 (vs), 1605 (vs), 1570, 1065, 1050, 1000 (s), 890 cm^{-1}; ^1H NMR ($CDCl_3$): Z δ 10.31 (s, 1 H), 7.40 (s, 1 H), 6.73 (s, 1 H), 3.03–1.63 (m, 6 H), E δ 10.17 (s, 1 H), 6.46 (s, 1 H), 6.83 (s, 1 H), 3.03–1.63 (m, 6 H); MS, m/z (rel intensity) 156 (M^+, 80), 121 (78); HRMS, calcd for C_8H_9ClO 156.0342, found 156.0341.

The 2,4-dinitrophenylhydrazone of **22a** was obtained as purple prisms (91%) from ethyl acetate: mp 134–136 °C; HRMS calcd for $C_{14}H_{13}ClN_4O_4$ 336.0625, found 336.0610.

(*E*)- and (*Z*)-(3-Chloro-5-methyl-2-cyclohexenylidene)acetaldehyde (22b). The following is a modification of the patent literature.[9] To a stirred mixture of *N*-formylmorpholine (13.8 g, 0.117 mol) and trichloroethylene (20 mL) at 5 °C was added phosphorus oxychloride (13.8 g, 90 mmol) over 5 min. After stirring the resultant solution for 10 min at 20 °C, 3,5-dimethyl-2-cyclohexen-1-one (3.0 g, 24 mmol) was added dropwise. The mixture was then stirred at 20 °C for 1 h. Workup as for **22a** gave a 3:2 E/Z isomeric mixture of **22b** as yellow oil (3.0 g, 73%): IR (neat) 2960 (vs), 2740, 1660 (C=O), 1600 (vs), 1370, 1120 (vs), 1010, 890, 810, 750 cm^{-1}; ^1H NMR ($CDCl_3$) Z δ 10.26 (s, 1 H), 7.40 (s, 1 H), 5.76 (s, 1 H), 2.80–1.70 (m, 5 H), 1.1 (d, J = 5 Hz, CH_3), E δ 10.13 (s, 1 H), 6.43 (s, 1 H), 5.90 (s, 1 H), 2.80–1.20 (m, 5 H), 1.1 (d, 3 H, J = 5 Hz, CH_3); MS, m/z (rel intensity) 170 (M^+, 36), 155 (52), 135 (47); HRMS, calcd for $C_9H_{11}ClO$ 170.0498, found 170.0495.

The 2,4-dinitrophenylhydrazone of **22b** was obtained as purple prisms (93%) from ethyl acetate: mp 207–209 °C. Anal. Calcd for $C_{15}H_{15}ClN_4O_4$: C, 51.36; H, 4.28; N, 15.98. Found: C, 51.04; H, 4.22; N, 15.66.

(*E*)- and (*Z*)-(1*S*-*cis*)-(2-Chloro-6,6-dimethylbicyclo[3.1.1]hept-2-en-4-ylidene)acetaldehyde (26). To a stirred mixture of *N*-formylmorpholine (6.9 g, 60 mmol) and trichloroethylene (10 mL) at 5 °C was added phosphorus oxychloride (7 g, 45.8 mmol) over 5 min. After stirring the resultant solution for 10 min at 20 °C, (1S)-(–)-verbenone (1.5 g, 10 mmol) was added dropwise at 15–20 °C. The mixture was then stirred at 20 °C for 2 h. Workup as for **22a** afforded a 3:2 E/Z isomeric mixture of **26** as a yellow oil (1.87 g, 95%): IR (neat) 2960 (s), 2870, 1660 (C=O), 1600, 1580, 1110, 885, 875, 740 cm^{-1}; ^1H NMR ($CDCl_3$) Z δ 10.20 (d, J = 7.5 Hz, 1 H), 7.20 (s, 1 H), 5.71 (d, J = 7.5 Hz, 1 H), 2.90–1.20 (m, 7 H), 1.00 (s, CH_3), E δ 10.12 (d, J = 7.5 Hz, 1 H), 6.3 (s, 1 H), 5.81 (d, J = 7.5 Hz, 1 H), 2.90–1.20 (m, 7 H), 1.00 (s, CH_3); MS, m/z (rel intensity) 196 (M^+, 9), 181 (57), 161 (80); HRMS, calcd for $C_{11}H_{16}ClO$ 196.0655, found 196.0662.

The 2,4-dinitrophenylhydrazone of **26** was obtained as purple prisms (93%) form ethyl acetate: mp 196–198 °C. Anal. Calcd for $C_{17}H_{17}ClN_4O_4$: C, 54.18; H, 4.52; N, 14.87. Found: C, 54.06; H, 4.47; N, 14.50.

(3-Chloro-5-methyl-2-cyclohexylidene)acetaldehyde Dimethyl Acetal (23a). To a solution of sodium methoxide (0.051 g, 0.94 mmol) in methanol (2 mL) was added **22b** (0.16 g, 0.94 mmol). The mixture was stirred at 25 °C for 1 h. Evaporation under reduced pressure gave a residue which was extracted with diethyl ether. The ethereal layer was evaporated to give a 2:1 E/Z isomeric mixture of **23a** as a yellow oil (0.16 g, 79%): IR (neat) 2960, 1660 (C=O), 1605, 1130, 890, 805 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.69, (br s, 1 H, Z isomer), 6.26 (br s, 1 H, E isomer), 5.43–5.10 (m, 2 H), 3.36 (s, 6 H), 2.85–1.40 (m, 5 H), 1.05 (d, J = 5 Hz, 3 H); MS, m/z (rel intensity) 216 (M^+, 14), 185 (100), 169 (87); HRMS, calcd for $C_{11}H_{17}ClO_2$ 216.0917, found 216.0902.

(3-Chloro-5,5-dimethyl-2-cyclohexylidene)acetaldehyde Dimethyl Acetal (23b). To a solution of sodium methoxide (23 mg, 0.42 mmol) in methanol (1 mL) was added **22c** (78 mg, 0.42 mmol); the mixture was stirred at 20 °C for 7 h. Evaporation of the methanol gave a residue which was extracted with diethyl ether. Evaporation of the ether gave a 3:2 E/Z isomeric mixture of **23b** as a yellow oil (74 mg, 76%): ^1H NMR ($CDCl_3$) δ 6.67 (br s, 1 H, Z isomer), 6.23 (br s, 1 H, E isomer), 5.53–5.00 (m, 2 H), 3.34 (s, 6 H), 2.40–1.85 (m, 4 H), 0.95 (s, 6 H); MS, m/z (rel intensity) 230 (M^+, 1), 198 (37), 183 (97), 169 (38); HRMS, calcd for $C_{12}H_{19}ClO_2$ 230.1074, found 230.1078. This mixture of E and Z isomers of **23b** closely resembled that prepared by the method of Traas, Boelens, and Takken.[10]

1-Anilino-5,5-dimethyl-3-(2-phenyliminoethylidene)cyclohex-1-ene (20). To a solution of aniline (93 mg, 1.0 mmol) in diethyl ether (5 mL) was added **22c** (94 mg, 0.5 mmol). The solution was stirred at 25 °C for 7 h. The resultant precipitate was filtered, washed with diethyl ether, and dried to give **20** as dark purple needles (0.14 g, 88%): mp 135–137 °C; IR ($CHBr_3$) 1670, 1600, 1510, 1470, 970 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50–6.15 (m, 14 H), 3.60–2.40 (m, 4 H), 1.03 (s, 6 H); MS, m/z (rel intensity) 316 (M^+, 8), 301 (16), 93 (100); HRMS, calcd for $C_{22}H_{24}N_2$ 316.1940, found 316.1910.

Reaction of 4,6,6-Trimethyl-2-((trimethylsilyl)oxy)cyclohexa-1,3-diene (37) with *N*-Formylmorpholine and Phosphorus Oxychloride. To a stirred mixture of *N*-formylmorpholine (13.8 g, 0.117 mol) and trichloroethylene (20 mL) at 5 °C was added phosphorus oxychloride (13.8 g, 90 mol) over 5 min. After stirring the resultant solution for 10 min at 20 °C, diene **37** (3 g, 14 mmol) was added dropwise. The mixture was then stirred at 20 °C for 4 h. Methylene chloride (50 mL) was added, and the reaction mixture was then brought to pH 7 with a solution of sodium carbonate (25 g, 0.236 mol) in water (150 mL). The organic layer was separated, and the aqueous layer was extracted with methylene chloride (3 × 100 mL); the combined organic layers were washed with water (120 mL) and dried over magnesium sulfate (20 g). Evaporation of the solvent and purification of the residue by column chromatography on silica gel using methylene chloride as eluent afforded first **40** as a yellow oil (0.22 g, 8.5%) and then a 3:2 E/Z isomeric mixture of **22c**, also as a yellow oil (2.3 g, 89%).

For **40**: IR (neat) 2940, 2840, 1655, 1640, 900, 855, 820, 800 cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.19 (s, 1 H), 5.73 (br s, 1 H), 1.96 (br s, 2 H), 1.76 broad (s, 3 H), 1.05 (s, 6 H); MS, m/z (rel intensity) 184, (34), 169 (8), 155 (48), 141 (74), 105 (100); HRMS, calcd for $C_{10}H_{13}ClO$: 184.0655, found 184.0647.

For **22c**: ^1H NMR data were identical with those previously reported.[10] MS, m/z (rel intensity) 184 (M^+, 53), 169 (90), 149 (76); HRMS, calcd for $C_{10}H_{13}ClO$ 184.0655, found 184.0660.

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