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Haval–Argade contrathermodynamic rearrangement of alkylidenesuccinimides to alkylmaleimides via the corresponding isoimides: a general approach to alkyl and dialkyl substituted maleimides☆

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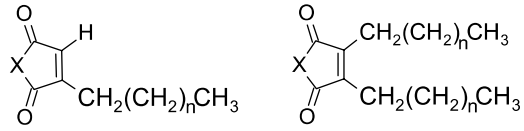
Abstract—A simple and efficient access to alkyl and dialkyl substituted maleimides has been demonstrated via the new contrathermodynamic rearrangement of (*E*)-alkylidenesuccinimides to alkylmaleimides. The (*E*)-alkylidenesuccinimides obtained from the Wittig-condensation of *N*-arylmaleimide with aliphatic aldehydes on regioselective hydrolysis furnished the corresponding (*E*)-alkylidenesuccinanilic acids in 95–98% yields. The β-alkylidenesuccinanilic acids on treatment with cyanuric chloride in the presence of triethylamine gave the corresponding β-alkylisomaleimides in 78–80% yields via the β-alkylideneisosuccinimides with the exocyclic to endocyclic carbon–carbon double bond migration. The kinetically controlled products alkylisomaleimides in refluxing acetic acid furnished the thermodynamically controlled alkylmaleimides in 98% yield. The Wittig condensation of alkyl substituted isomaleimides/maleimides with aliphatic aldehydes gave the desired dialkyl substituted maleimides in high yields. A conversion of α-methylenesuccinanilic acids to α-methylisomaleimides has also been described, with 90% yield.

1. Introduction

The cyclic anhydrides and imides are the compounds of choice for all chemists from both the basic and applied point of view for multiple purposes. The vast array of nucleophilic reactions undergone by symmetrical and unsymmetrical maleic anhydrides and maleimides confer on them a high synthetic potential. As such, a large number of maleic anhydrides and maleimides have been extensively used in the synthesis of natural and unnatural bioactive heterocyclic compounds,[1] structurally interesting compounds highlighting regiochemical dichotomy[2] and several types of polymers with tailored material characteristics.[3] Maleic anhydrides and maleimides bearing both hydrophilic groups and hydrophobic parts are very important for their bioactivities and material properties[4] (Fig. 1). Several alkylmethyl substituted maleic anhydrides such as chaetomellic acids A and B, aspergillus acids A–D, maleic anhydride segment of tautomycin and tyromycin A are known in the literature[5,6] as bioactive natural products and one can surmise that nature might be designing them by employing the condensation of pyruvic acid with the other respective carboxylic acids. Several elegant routes to alkylmethylmaleic anhydrides have been reported in the past decade.[6] To the best of our knowledge, to date no natural product with a simple monoalkyl or dialkyl substituted maleic anhydride moiety is known in the literature. Only one method for the synthesis of monoalkyl substituted maleic anhydrides is known—by the Heck reaction using palladium-catalyzed dicarbonylation of terminal acetylenes.[7] The use of poisonous carbon monoxide is a drawback of this simple one-step approach. The dialkyl substituted maleic anhydrides have been designed using the Grignard coupling reactions with dimethyl acetylenedicarboxylate at −78 °C followed by



X = O, NAr, n = 0 - 12

Figure 1. Alkyl and dialkyl substituted maleic anhydrides and imides.

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Keywords: Maleimides; Wittig coupling; Isomaleimides; Contrathermodynamic rearrangement; Alkyl and dialkylmaleimides.
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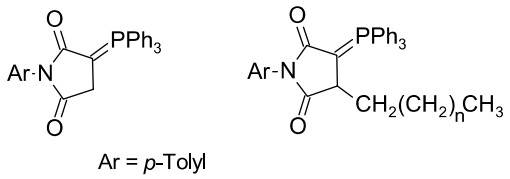


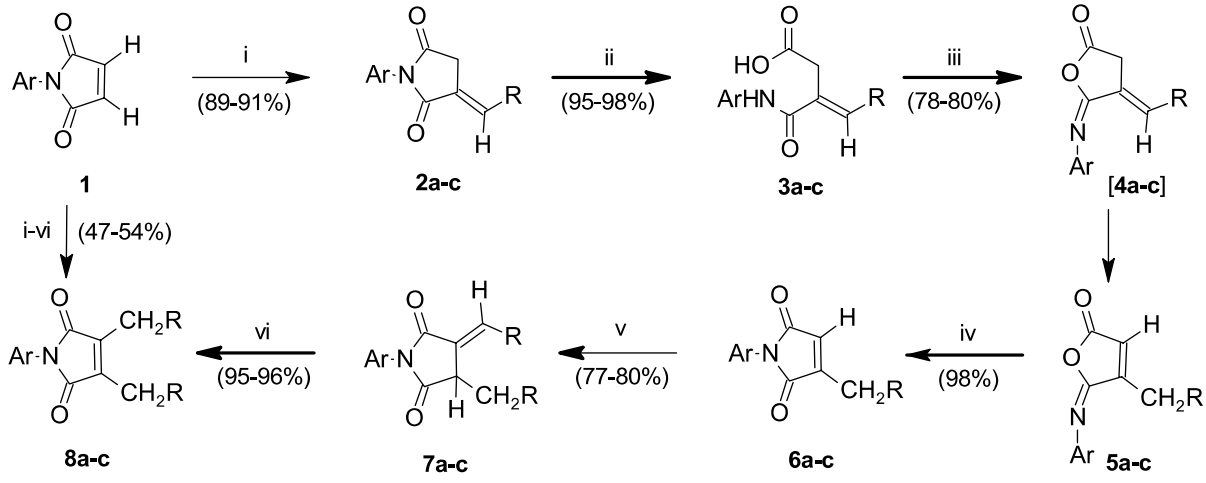
Figure 2. Triphenylphosphine and maleimide adducts (Wittig adducts).

trapping the *cis*-enolate with alkyl halides.[8] The low temperature reactions, lower reactivities of *cis*-enolates at that temperature and contamination of *trans*-enolates are the limitations of this approach. Hence, development of a new practical approach to the alkyl and dialkyl substituted maleic anhydrides and maleimides is still a useful and challenging task of current interest. In continuation of our studies on cyclic anhydrides chemistry,[9] now we herein report an easy approach to monoalkyl and dialkyl substituted maleimides via the contrathermodynamic (*E*)-alkylidenesuccinimides to alkylmaleimides rearrangement as a key reaction.

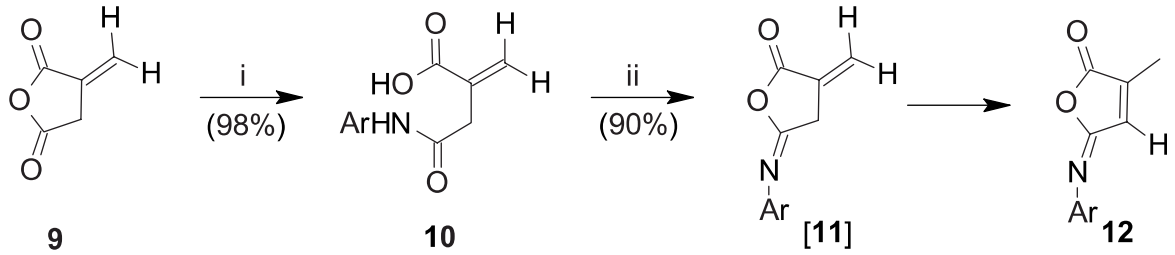
2. Results and discussion

The formation of maleimide–triphenylphosphine adduct is well known[10] (Fig. 2) and we felt that the stepwise activation of two vinylic protons in maleimide as Wittig adducts would provide an efficient approach to alkylmaleimides and dialkylmaleimides. In this context, starting from *N*-*p*-tolylmaleimide (**1**), we prepared the (*E*)-alkylidenesuccinimides **2a–c** in 89–91% yield[11] (Scheme 1). We thought that trisubstituted exocyclic carbon–carbon double bond in compounds **2** will migrate easily to form the trisubstituted endocyclic compounds **6** for the two reasons, viz. (i) exocyclic to endocyclic carbon–carbon double bond migrations are generally more easy and (ii) the endocyclic trisubstituted carbon–carbon double bond will be in conjugation with two imide carbonyls.[12] We tried several reagents and reaction conditions for the conversion of **2–6**, but all our attempts met with failure. The conversion of **2–6** under basic conditions (Et_3N, Pyridine, DBU, NaH, *t*-BuO^-K^+, *t*-BuLi), under the thermal conditions (heat 150–200 °C, tetralin reflux) and under the transition metal catalyzed isomerization conditions [$RuCl_3$, $HRuCl(PPh_3)_3$, $RhCl_3$, $HRhCl(PPh_3)_3$] were fruitless. We learnt from these experiments that such type of (*E*)-alkylidenesuccinimides **2** to alkylmaleimides **6** conversion is a difficult process. The compounds **2a–c** could be thermodynamically more stable due to the extra stability of carbon–carbon double bond with (*E*)-geometry, than the corresponding compounds **6a–c**. We planned with reason and decided to alter the imide dicarbonyl symmetry of **2** for such type of double bond migrations. The amic/anilic acids under kinetically controlled dehydration conditions are known to furnish the corresponding isoimides.[13] We felt that preparation of isoimides would be helpful for such a carbon–carbon double bond migration as the isomaleimides are expected to be more stable than the corresponding alkylidineisosuccinimides due to the extension of π-cloud conjugation from the aryl ring to the butyroiminolide carbonyl group. The highly regioselective aqueous lithium hydroxide induced hydrolysis of **2** exclusively furnished the β-alkylidenesuccinanilic acids **3** in 95–98% yields.

Cyanuric chloride is a decent dehydrating agent for such type of kinetic dehydrations[13] and the treatment of acids **3** with cyanuric chloride in the presence of triethyl amine as a base at room temperature directly furnished the expected *anti*-β-alkylisomaleimides **5** in 78–80% yields. Both the dehydrative cyclizations of acids **3** to form the intermediates β-alkylideneisosuccinimides **4** (which could not be isolated) and the abstraction of the α-methylene proton on intermediate **4** to form the β-alkyl isomaleimides **5** took place in one-pot. Our hypothesis turned out to be correct and to the best of our knowledge this is the first example of carbanion generation on an isoimide skeleton, though in situ, and its application for the facile carbon framework rearrangement. The structures of isomaleimides **5a–c** were unambiguously established on the basis of lactone carbonyl (1794–1798 cm^{-1}) and imine (1676–1678 cm^{-1}) stretching frequencies in IR-spectra, appropriate ^1H NMR data and the presence of imine carbon atom (δ 140.9–141.0) in ^{13}C NMR spectra. We could very easily convert these kinetically controlled alkylisomaleimides **5a–c** to the



Scheme 1. Reagents, conditions and yields: (i) PPh_3, THF, RCHO, reflux, 10 h (89–91%); (ii) aq 2 N LiOH, THF, 0 °C to rt, 5 h, (95–98%); (iii) cyanuric chloride, NEt_3, DCM, 0 °C to rt, 8 h (78–80%); (iv) AcOH, reflux, 5 h (98%); (v) PPh_3, AcOH, RCHO, reflux, 18 h (77–80%); (vi) NEt_3 + THF (1:1), reflux, 48 h (95–96%).



Scheme 2. Reagents, conditions and yields: (i) Et_2O, $ArNH_2$, rt, 1 h (98%); (ii) cyanuric chloride, NEt_3, DCM, 0 °C to rt, 8 h (90%).

desired corresponding thermodynamically more stable alkylmaleimides **6a–c** in 98% yield, by just refluxing them in glacial acetic acid for five hours. Both the opening of iminobutenolides **5** with acetic acid to form the mix anhydride intermediates and the intramolecular cyclization via the amide nitrogen lone pair to form the compounds **6** took place in one-pot. We feel that these monoalkyl substituted maleimides **6** will be potential precursors for several bioactive natural products containing butenolide/butyrolactone and butyrolactam core with fatty alkyl chain substituents.[14] Both the alkylisomaleimides **5** and alkylmaleimides **6** on treatment with refluxing acetic acid–sodium acetate mixture or on treatment with triethylamine in THF reverted to the more stable (*E*)-alkylidenesuccinimides **2** in quantitative yield, proving that in these systems the endocyclic to exocyclic carbon–carbon double bond migrations are more facile. These observations revealed and confirmed that the order of thermodynamic stability for these imides and isoimides is **2**>**6**>**5**>**4** and what we have accomplished was the contrathermodynamic rearrangement of exoimides **2** to endoimides **6** via the isoimides **4** and **5**. Finally, with the application of our earlier developed synthetic protocol[6f] for the synthesis of chaetomellic acid A, we could very easily transform the alkyl substituted maleimides to the symmetrically dialkyl substituted maleimides **8** via the intermediates **7** in very good yields. As expected the alkylisomaleimides on triphenylphosphine induced Wittig condensation with aliphatic aldehydes in refluxing acetic acid also furnished the imides **8** via the intermediates **6** and **7** in 77–80% yield. In the present 4-step approach the alkylmaleimides were obtained in 65–70% overall yields, while in the 5-step approach, the dialkylsubstituted maleimides were obtained in 48–55% overall yields. In the present synthetic sequence, the stepwise use of two different aliphatic aldehydes would provide a way to the unsymmetrically dialkylsubstituted maleimides. The hydrolysis of alkylsubstituted maleimides **6** under acidic conditions followed by the dehydration to the corresponding alkylmaleic anhydrides and the hydrolysis of dialkylmaleimides to the corresponding dialkylmaleic anhydrides is well known in the literature.[6f,7,9i]

In the above mentioned strategy, we have proved that the α-protons on the inisolable intermediate alkylideneisosuccinimides **4** are accessible for such type of rearrangements. We planned to verify the accessibility of the corresponding β-protons in α-alkylideneisosuccinimides. In this context, we performed the regioselective ring opening of itaconic anhydride (**9**) with *p*-toluidine and obtained the α-methylenesuccinanilic acid **10** in 98% yield (Scheme 2). The treatment of acid **10** with cyanuric chloride in the presence of triethylamine also gave α-methylisomaleimide **12** in 90% yield via the intermediate α-methyleneisosuccinimide **11**, proving that β-methylene protons can also be abstracted in a similar fashion for such type of *exo–endo* framework rearrangements.

3. Conclusion

In summary, we have demonstrated a simple and efficient approach to alkylmaleimides and dialkylmaleimides via the two Wittig coupling reactions, taking advantage for the first time of kinetically controlled isoimides as intermediates to enforce the difficult migration of exocyclic carbon–carbon double bonds to the endocyclic position (**2a–c** to **6a–c**). We have also demonstrated that in the present strategy, both the α- and β-methylene protons on isosuccinimide skeleton are accessible for such type of exocyclic to endocyclic carbon–carbon double bond migrations. The present Haval–Argade contrathermodynamic rearrangement is noteworthy and lots of new chemistry will be possible from this important isoimide functionality. The present practical approach with scale up potential is general in nature and it will be useful to design a large number of analogs and congeners of alkylmaleimides and dialkylmaleimides of interest, to a large section of the chemists' community. We also feel that the present approach will be useful to design carbocyclic compounds like byssochlamic acid and its analogs. The present results will also be of interest to chemists studying such type of *exo–endo* carbon–carbon double bond isomerization reactions.

4. Experimental

4.1. General

Commercially available cyclic anhydrides, aromatic amines, aliphatic aldehydes and triphenylphosphine were used. Freshly recrystallized cyanuric chloride (CCl_4) was used. Melting points are uncorrected. Column chromatographic separations were carried out on ACME silica gel (60–120 mesh). FT-IR spectra were recorded on a FT-IR-8300 Shimadzu spectrometer. ^{1}H NMR spectra were recorded in $CDCl_3$ using TMS as internal standard and in DMSO-d_6 on a Bruker AC 200, MSL 300 and Bruker DRX 500 NMR spectrometers (200, 300 and 500 MHz, respectively). ^{13}C NMR spectra were recorded on a Bruker AC 200, MSL 300 and Bruker DRX 500 NMR spectrometers (50, 75 and 125 MHz, respectively).

4.2. General procedure for *N*-*p*-tolyl-3(*E*)-alkylidene-succinimides 2a–c

A solution of *N*-*p*-tolylmaleimide (**1**, 50 mmol) and triphenylphosphine (50 mmol) in THF (125 mL) was stirred at room temperature for 30 min. To the reaction mixture was added aliphatic aldehyde (75 mmol) and it was refluxed for 10 h. The THF was distilled off in vacuo at 50 °C and the residue was purified by silica gel column chromatography using a mixture of petroleum ether and ethyl acetate (9:1) to obtain the alkylidenesuccinimides **2a/b/c** in 89–91% yields.

4.2.1. 3-Hexylidene-1-*p*-tolyl-pyrrolidine-2,5-dione (2a). White solid (12.34 g, 91%), mp 112–113 °C (petroleum ether); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.90 (t, J=6 Hz, 3H), 1.22–1.45 (m, 4H), 1.53 (quintet, J=6 Hz, 2H), 2.23 (q, J=6 Hz, 2H), 2.37 (s, 3H), 3.37 (d, J=2 Hz, 2H), 6.93 (tt, J=8, 2 Hz, 1H), 7.18 (d, J=8 Hz, 2H), 7.27 (d, J=8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 13.7, 20.9, 22.2, 27.5, 29.6, 31.2, 31.8, 125.1, 126.0, 129.2, 129.4, 138.1, 139.6, 168.7, 173.0; MS (*m*/*e*) 271, 242, 228, 214, 200, 189, 172, 133, 107, 95, 81, 67, 53; IR (Nujol) ν_{max} 1771, 1749, 1712, 1691, 1676 cm^{-1}. Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.24; H, 7.80; N, 5.16. Found: C, 75.11; H, 7.92; N, 5.07.

4.2.2. 3-Decylidene-1-*p*-tolyl-pyrrolidine-2,5-dione (2b). White solid (14.54 g, 89%), mp 106–108 °C (petroleum ether); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.88 (t, J=6 Hz, 3H), 1.27 (bs, 12H), 1.52 (quintet, J=6 Hz, 2H), 2.23 (q, J=6 Hz, 2H), 2.37 (s, 3H), 3.37 (d, J=2 Hz, 2H), 6.93 (tt, J=8, 2 Hz, 1H), 7.18 (d, J=8 Hz, 2H), 7.27 (d, J=8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.0, 21.1, 22.6, 28.0, 29.18, 29.24, 29.31, 29.37, 29.9, 31.8, 32.0, 125.2, 126.2, 129.3, 129.7, 138.4, 140.0, 169.0, 173.2; IR (Nujol) ν_{max} 1771, 1709, 1676, 1466 cm^{-1}. Anal. Calcd for $C_{21}H_{29}NO_2$: C, 77.02; H, 8.93; N, 4.28. Found: C, 76.89; H, 9.02; N, 4.16.

4.2.3. 3-Tetradecylidene-1-*p*-tolyl-pyrrolidine-2,5-dione (2c). White solid (17.06 g, 89%), mp 58–60 °C (petroleum ether); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.88 (t, J=6 Hz, 3H), 1.25 (bs, 20H), 1.55 (quintet, J=6 Hz, 2H), 2.25 (q, J=6 Hz, 2H), 2.39 (s, 3H), 3.38 (d, J=2 Hz, 2H), 6.95 (tt, J=8, 2 Hz, 1H), 7.20 (d, J=8 Hz, 2H), 7.28 (d, J=8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.7, 20.8, 22.3, 27.9, 29.1, 29.2, 29.3 (7×CH_2), 29.5, 31.8, 125.4, 125.9, 129.2, 129.5, 137.8, 139.1, 168.5, 172.6; MS (*m*/*e*) 383, 355, 257, 228, 215, 202, 189, 172, 108, 95, 81; IR (Nujol) ν_{max} 1785, 1720, 1695, 1470 cm^{-1}. Anal. Calcd for $C_{25}H_{37}NO_2$: C, 78.28; H, 9.72; N, 3.65. Found: C, 78.19; H, 9.64; N, 3.60.

4.3. General procedure for *N*-*p*-tolyl-3(*E*)-alkylidene-succinanilic acids 3a–c

To a solution of alkylidenesuccinimides (**2a**–**c**, 40 mmol) in THF (50 mL) was added 2 N aqueous LiOH (50 mL) in a dropwise fashion at 0 °C and the reaction mixture was stirred for 5 h at room temperature. THF was distilled off in vacuo and the aqueous layer was acidified with 2 N HCl and extracted with ethyl acetate (3×50 mL). The combined organic layer was washed with water, brine and dried over Na_2SO_4. Concentration of the organic layer in vacuo gave the desired alkylidenesuccinanilic acids **3a**–**c** in 95–98% yields.

4.3.1. 3-*p*-Tolylcarbamoyl-non-3-enoic acid (3a). White solid (11.33 g, 98%), mp 143–145 °C (petroleum ether+ethyl acetate); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.87 (t, J=6 Hz, 3H), 1.20–1.40 (m, 4H), 1.47 (quintet, J=6 Hz, 2H), 2.27 (s, 3H), 2.37 (q, J=6 Hz, 2H), 3.38 (s, 2H), 7.06 (d, J=8 Hz, 2H), 7.16 (t, J=6 Hz, 1H), 7.33 (d, J=8 Hz, 2H), 8.01 (bs, 1H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 14.0, 20.6, 22.1, 28.0, 28.5, 31.1, 34.1, 119.0, 119.1, 129.2, 131.9, 137.0, 137.1, 168.3, 168.4; IR (Nujol) ν_{max} 2383, 2700–2500, 1682, 1657, 1597 cm^{-1}. Anal. Calcd for $C_{17}H_{23}NO_3$: C, 70.56; H, 8.01; N, 4.84. Found: C, 70.43; H, 7.96; N, 4.85.

4.3.2. 3-*p*-Tolylcarbamoyl-tridec-3-enoic acid (3b). White solid (13.24 g, 96%), mp 138–140 °C (petroleum ether+ethyl acetate); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.87 (t, J=6 Hz, 3H), 1.24 (bs, 12H), 1.47 (quintet, J=6 Hz, 2H), 2.28 (s, 3H), 2.39 (q, J=6 Hz, 2H), 3.38 (s, 2H), 7.07 (d, J=8 Hz, 2H), 7.18 (t, J=6 Hz, 1H), 7.34 (d, J=8 Hz, 2H), 7.96 (bs, 1H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 14.2, 20.6, 22.3, 28.3, 28.5, 28.6, 28.7, 28.9, 29.1, 29.2, 31.5, 119.0, 119.1, 129.2, 131.9, 137.0, 137.1, 168.4, 168.5; IR (Nujol) ν_{max} 3420, 2700–2500, 1682, 1661, 1597 cm^{-1}. Anal. Calcd for $C_{21}H_{31}NO_3$: C, 73.00; H, 9.04; N, 4.05. Found: C, 73.12; H, 9.13; N, 4.16.

4.3.3. 3-*p*-Tolylcarbamoyl-heptadec-3-enoic acid (3c). White solid (15.21 g, 95%), mp 126–128 °C (petroleum ether); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.87 (t, J=6 Hz, 3H), 1.24 (bs, 20H), 1.47 (quintet, J=6 Hz, 2H), 2.28 (s, 3H), 2.38 (q, J=6 Hz, 2H), 3.38 (s, 2H), 7.07 (d, J=8 Hz, 2H), 7.17 (t, J=6 Hz, 1H), 7.33 (d, J=8 Hz, 2H), 7.94 (bs, 1H); ^{13}C NMR ($CDCl_3$+DMSO-d_6, 50 MHz) δ 12.6, 19.2, 20.9, 27.0, 27.3, 27.5, 27.6, 27.7, 27.9 (5×CH_2), 30.2, 33.1, 117.8, 125.4, 127.5, 130.7, 135.2, 143.6, 167.0, 167.4; IR (Nujol) ν_{max} 3411, 2700–2500, 1688, 1660, 1599 cm^{-1}. Anal. Calcd for $C_{25}H_{39}NO_3$: C, 74.77; H, 9.79; N, 3.49. Found: C, 74.69; H, 9.82; N, 3.51.

4.4. General procedure for *N*-*p*-tolylalkylisomaleimides 5a–c

To a slurry of alkylidenesuccinanilic acids (**3a**–**c**, 30 mmol) in DCM (50 mL) was added triethylamine (90 mmol) in a dropwise fashion with constant stirring at 0 °C. To the resulting reaction mixture was added a solution of cyanuric chloride (33 mmol) in DCM (50 mL) and the reaction mixture was further stirred under argon atmosphere for 8 h at room temperature. The reaction mixture was concentrated in vacuo and residue was dissolved in ethyl acetate (50 mL). The organic layer was washed with water, 5% aqueous sodium bicarbonate, brine and dried over Na_2SO_4. The ethyl acetate layer was concentrated in vacuo and the crude product was purified by silica gel column chromatography using a mixture of petroleum ether and ethyl acetate (9:1) to obtain pure *N*-*p*-tolylalkylisomaleimides **5a**–**c** in 78–80% yields.

4.4.1. 4-Hexyl-5-*p*-tolylimino-5*H*-furan-2-one (5a). Thick oil (6.50 g, 80%), ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.90 (t, J=6 Hz, 3H), 1.35 (bs, 6H), 1.69 (quintet, J=6 Hz, 2H), 2.35 (s, 3H), 2.64 (t, J=6 Hz, 2H), 6.29 (s, 1H), 7.17 (d, J=8 Hz, 2H), 7.33 (d, J=8 Hz, 2H); ^{13}C NMR ($CDCl_3$,

50 MHz) δ 13.9, 21.0, 22.4, 26.2, 27.3, 28.8, 31.3, 121.0, 125.3, 129.4, 137.1, 140.9, 150.1, 159.7, 167.1; IR (neat) ν_{max} 1798, 1678, 1622, 1506 cm^{-1}. Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.24; H, 7.80; N, 5.16. Found: C, 75.12; H, 7.93; N, 5.02.

4.4.2. 4-Decyl-5-*p*-tolylimino-5*H*-furan-2-one (5b). White solid (7.67 g, 78%), mp 53–55 °C (petroleum ether); ^1H NMR ($CDCl_3$, 200 MHz) δ 0.87 (t, $J=6$ Hz, 3H), 1.25 (bs, 14H), 1.68 (quintet, $J=6$ Hz, 2H), 2.35 (s, 3H), 2.64 (t, $J=6$ Hz, 2H), 6.29 (s, 1H), 7.17 (d, $J=8$ Hz, 2H), 7.33 (d, $J=8$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.1, 21.1, 22.7, 26.3, 27.4, 29.1, 29.2, 29.3, 29.4, 29.6, 31.9, 121.1, 125.4, 129.5, 137.1, 141.0, 150.2, 159.8, 167.2; IR ($CHCl_3$) ν_{max} 1798, 1678, 1622, 1506 cm^{-1}. Anal. Calcd for $C_{21}H_{29}NO_2$: C, 77.02; H, 8.93; N, 4.28. Found: C, 77.11; H, 9.04; N, 4.33.

4.4.3. 4-Tetradecyl-5-*p*-tolylimino-5*H*-furan-2-one (5c). White solid (8.96 g, 78%), mp 58–60 °C (petroleum ether); ^1H NMR ($CDCl_3$, 200 MHz) δ 0.87 (t, $J=6$ Hz, 3H), 1.25 (bs, 22H), 1.68 (quintet, $J=6$ Hz, 2H), 2.35 (s, 3H), 2.64 (t, $J=6$ Hz, 2H), 6.29 (s, 1H), 7.17 (d, $J=8$ Hz, 2H), 7.33 (d, $J=8$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.1, 21.1, 22.7, 26.3, 27.4, 29.1, 29.2, 29.3, 29.4, 29.6 ($5\times CH_2$), 31.9, 121.1, 125.4, 129.5, 137.1, 141.0, 150.2, 159.8, 167.2; IR ($CHCl_3$) ν_{max} 1794, 1676, 1620, 1506 cm^{-1}. Anal. Calcd for $C_{25}H_{37}NO_2$: C, 78.28; H, 9.72; N, 3.65. Found: C, 78.33; H, 9.59; N, 3.60.

4.4.4. 3-Methyl-5-*p*-tolylimino-5*H*-furan-2-one (12). This compound was obtained in 90% yield by using the same procedure as used for the synthesis of compounds **5a–c**; off white solid; mp 115–116 °C (petroleum ether); ^1H NMR ($CDCl_3$, 300 MHz) δ 2.15 (s, 3H), 2.36 (s, 3H), 7.02 (s, 1H), 7.19 (d, $J=9$ Hz, 2H), 7.32 (d, $J=9$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 10.7, 21.0, 125.0, 129.4, 136.5, 136.9, 138.7, 141.2, 148.9, 168.7; IR (Nujol) ν_{max} 1778, 1674, 1599, 1462 cm^{-1}. Anal. Calcd for $C_{12}H_{11}NO_2$: C, 71.62; H, 5.51; N, 6.96. Found: C, 71.77; H, 5.48; N, 6.93.

4.5. General procedure for *N*-*p*-tolylalkylmaleimides 6a–c

A solution of *N*-*p*-tolylalkylisomaleimides (**5a–c**, 20 mmol) in glacial acetic acid (50 mL) was refluxed for 5 h. Acetic acid was distilled off in vacuo at 50 °C and the residue was dissolved in ethyl acetate. The organic layer was washed with water, aqueous sodium bicarbonate, brine and dried over Na_2SO_4. The organic layer was concentrated in vacuo and the obtained residue, on silica gel column chromatographic purification using petroleum ether and ethyl acetate (9.5:0.5), gave *N*-*p*-tolylalkylmaleimides **6a–c** in 98% yields.

4.5.1. 3-Hexyl-1-*p*-tolyl-pyrrole-2,5-dione (6a). White solid (5.31 g, 98%), mp 70–72 °C (petroleum ether+ethyl acetate); ^1H NMR ($CDCl_3$, 200 MHz) δ 0.89 (t, $J=6$ Hz, 3H), 1.15–1.50 (m, 6H), 1.64 (quintet, $J=6$ Hz, 2H), 2.36 (s, 3H), 2.50 (dt, $J=6$, 2 Hz, 2H), 6.40 (t, $J=2$ Hz, 1H), 7.10–7.30 (m, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.0, 21.1, 22.4, 25.4, 27.0, 28.8, 31.4, 125.8, 126.2, 128.9, 129.6, 137.6, 150.3, 169.9, 170.5; IR ($CHCl_3$) ν_{max} 1773, 1713, 1638, 1516 cm^{-1}. Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.24; H, 7.80; N, 5.16. Found: C, 75.20; H, 7.73; N, 5.11.

4.5.2. 3-Decyl-1-*p*-tolyl-pyrrole-2,5-dione (6b). White solid (6.40 g, 98%), mp 58–60 °C (petroleum ether+ethyl acetate); ^1H NMR ($CDCl_3$, 200 MHz) δ 0.87 (t, $J=6$ Hz, 3H), 1.26 (bs, 14H), 1.64 (quintet, $J=6$ Hz, 2H), 2.36 (s, 3H), 2.50 (dt, $J=6$, 2 Hz, 2H), 6.40 (t, $J=2$ Hz, 1H), 7.10–7.30 (m, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.1, 21.1, 22.6, 25.5, 27.0, 29.2, 29.3, 29.4, 29.5, 30.1, 31.9, 125.8, 126.2, 128.9, 129.7, 137.6, 150.3, 170.0, 170.6; IR ($CHCl_3$) ν_{max} 1773, 1713, 1638, 1516 cm^{-1}. Anal. Calcd for $C_{21}H_{29}NO_2$: C, 77.02; H, 8.93; N, 4.28. Found: C, 76.95; H, 8.88; N, 4.21.

4.5.3. 3-Tetradecyl-1-*p*-tolyl-pyrrole-2,5-dione (6c). White solid (7.52 g, 98%), mp 72–74 °C (petroleum ether+ethyl acetate); ^1H NMR ($CDCl_3$, 200 MHz) δ 0.87 (t, $J=6$ Hz, 3H), 1.25 (bs, 22H), 1.64 (quintet, $J=6$ Hz, 2H), 2.36 (s, 3H), 2.50 (dt, $J=6$, 2 Hz, 2H), 6.40 (t, $J=2$ Hz, 1H), 7.10–7.30 (m, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.1, 21.1, 22.7, 25.5, 27.1, 29.2, 29.3, 29.5, 29.6 ($6\times CH_2$), 31.9, 125.9, 126.2, 128.9, 129.7, 137.7, 150.3, 169.9, 170.6; IR ($CHCl_3$) ν_{max} 1773, 1713, 1638, 1516 cm^{-1}. Anal. Calcd for $C_{25}H_{37}NO_2$: C, 78.28; H, 9.72; N, 3.65. Found: C, 78.22; H, 9.81; N, 3.54.

4.6. General procedure for *N*-*p*-tolyl-2-alkylidene-3-alkylsuccinimides 7a–c

A solution of *N*-*p*-tolylalkylmaleimides (**6a–c**, 10 mmol), triphenylphosphine (10 mmol) and aliphatic aldehyde (15 mmol) in glacial acetic acid (30 mL) was refluxed for 18 h with constant stirring. Acetic acid was distilled off in vacuo at 50 °C and the residue was dissolved in ethyl acetate (100 mL). The organic layer was washed with water, brine and dried over Na_2SO_4. Concentration of the organic layer in vacuo followed by silica gel column chromatographic purification of the residue using petroleum ether and ethyl acetate (9:1) gave *N*-*p*-tolyl-2-alkylidene-3-alkylsuccinimides **7a–c** in 77–80% yields.

The above compounds were also obtained from *N*-*p*-tolylalkylisomaleimides **5a–c** using the same procedure.

4.6.1. 3-Hexyl-4-hexylidene-1-*p*-tolyl-pyrrolidine-2,5-dione (7a). Off white solid (2.85 g, 80%), mp 69–70 °C (petroleum ether+ethyl acetate); ^1H NMR ($CDCl_3$, 200 MHz) δ 0.86 (t, $J=6$ Hz, 3H), 0.91 (t, $J=6$ Hz, 3H), 1.15–1.45 (m, 12H), 1.53 (quintet, $J=6$ Hz, 2H), 1.75–1.98 (m, 1H), 1.98–2.15 (m, 1H), 2.28 (q, $J=8$ Hz, 2H), 2.38 (s, 3H), 3.51 (unresolved multiplet, 1H), 6.93 (dt, $J=8$, 2 Hz, 1H), 7.17 (d, $J=8$ Hz, 2H), 7.27 (d, $J=8$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 13.9, 14.0, 21.2, 22.4, 22.5, 24.6, 28.1, 29.2, 29.3, 30.7, 31.5, 31.6, 42.5, 126.2, 129.0, 129.3, 129.7, 138.4, 140.3, 169.3, 176.9; IR ($CHCl_3$) ν_{max} 1767, 1709, 1670, 1516 cm^{-1}. Anal. Calcd for $C_{23}H_{33}NO_2$: C, 77.70; H, 9.36; N, 3.94. Found: C, 77.79; H, 9.43; N, 3.72.

4.6.2. 3-Decyl-4-decylidene-1-*p*-tolyl-pyrrolidine-2,5-dione (7b). Off white solid (3.62 g, 78%), mp 71–73 °C (petroleum ether+ethyl acetate); ^1H NMR ($CDCl_3$, 200 MHz) δ 0.87 (t, $J=6$ Hz, 6H), 1.25 (bs, 28H),

1.40–1.60 (m, 2H), 1.75–2.15 (m, 2H), 2.27 (q, $J=8$ Hz, 2H), 2.37 (s, 3H), 3.50 (unresolved multiplet, 1H), 6.92 (dt, $J=8$, 2 Hz, 1H), 7.17 (d, $J=8$ Hz, 2H), 7.27 (d, $J=8$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.1, 21.2, 22.6, 24.7, 28.5, 29.3, 29.4, 29.5 (11×CH_2), 30.7, 31.9, 42.5, 126.2, 129.0, 129.4, 129.7, 138.4, 140.3, 169.2, 176.8; IR (Nujol) ν_{max} 1769, 1719, 1670, 1516 cm^{-1}. Anal. Calcd for $C_{31}H_{49}NO_2$: C, 79.60; H, 10.56; N, 2.99. Found: C, 79.52; H, 10.44; N, 3.07.

4.6.3. 3-Tetradecyl-4-tetradecylidene-1-*p*-tolyl-pyrrolidine-2,5-dione (7c). Off white solid (4.48 g, 77%), mp 73–75 °C (petroleum ether+ethyl acetate); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.80–0.90 (m, 6H), 1.10–1.40 (m, 44H), 1.45–1.55 (m, 2H), 1.80–1.95 (m, 1H), 1.95–2.10 (m, 1H), 2.20–2.33 (m, 2H), 2.37 (s, 3H), 3.50 (unresolved multiplet, 1H), 6.91 (dt, $J=8$, 2 Hz, 1H), 7.17 (d, $J=10$ Hz, 2H), 7.26 (d, $J=10$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.1, 21.2, 22.7, 24.7, 28.5, 29.3–29.6 (21×CH_2), 30.8, 31.9, 42.5, 126.2, 129.1, 129.4, 129.7, 138.5, 140.4, 169.3, 176.9; IR ($CHCl_3$) ν_{max} 1769, 1705, 1670, 1518 cm^{-1}. Anal. Calcd for $C_{39}H_{65}NO_2$: C, 80.77; H, 11.30; N, 2.42. Found: C, 80.67; H, 11.16; N, 2.53.

4.7. General procedure for *N*-*p*-tolyldialkylmaleimides 8a–c

To a stirred solution of *N*-*p*-tolyl-2-alkylidene-3-alkyl-succinimides (**7a–c**, 5 mmol) in THF (20 mL) was added triethylamine (20 mL) and the reaction mixture was refluxed for 48 h and then it was concentrated in vacuo. The residue was dissolved in ethyl acetate and the organic layer was washed with water, brine and dried over Na_2SO_4. Concentration of the organic layer in vacuo followed by silica gel column chromatographic purification of the residue using petroleum ether and ethyl acetate (9.5:0.5) gave *N*-*p*-tolyldialkylmaleimides **8a–c** in 95–96% yields.

4.7.1. 3,4-Dihexyl-1-*p*-tolyl-pyrrole-2,5-dione (8a). Thick oil (1.70 g, 96%), ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.89 (t, $J=6$ Hz, 6H), 1.15–1.45 (m, 12H), 1.57 (quintet, $J=6$ Hz, 4H), 2.36 (s, 3H), 2.44 (t, $J=8$ Hz, 4H), 7.22 (s, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.0, 21.1, 22.5, 23.9, 28.6, 29.3, 31.4, 125.7, 129.3, 129.5, 137.2, 141.1, 170.9; IR ($CHCl_3$) ν_{max} 1707, 1516, 1395 cm^{-1}. Anal. Calcd for $C_{23}H_{33}NO_2$: C, 77.70; H, 9.36; N, 3.94. Found: C, 77.79; H, 9.45; N, 3.99.

4.7.2. 3,4-Bis-decyl-1-*p*-tolyl-pyrrole-2,5-dione (8b). Thick oil (2.22 g, 95%), ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.87 (t, $J=6$ Hz, 6H), 1.25 (bs, 28H), 1.57 (quintet, $J=6$ Hz, 4H), 2.36 (s, 3H), 2.44 (t, $J=6$ Hz, 4H), 7.22 (s, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.0, 21.0, 22.6, 23.9, 28.6, 29.3, 29.5, 29.6 (3×CH_2), 31.9, 125.7, 129.3, 129.5, 137.1, 141.1, 170.9; IR (neat) ν_{max} 1711, 1516, 1389 cm^{-1}. Anal. Calcd for $C_{31}H_{49}NO_2$: C, 79.60; H, 10.56; N, 2.99. Found: C, 79.66; H, 10.47; N, 3.03.

4.7.3. 3,4-Ditetradecyl-1-*p*-tolyl-pyrrole-2,5-dione (8c). Thick oil (2.76 g, 95%), ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.87 (t, $J=6$ Hz, 6H), 1.25 (bs, 44H), 1.57 (quintet, $J=6$ Hz, 4H), 2.36 (s, 3H), 2.44 (t, $J=6$ Hz, 4H), 7.22 (s, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.1, 21.1, 22.7, 23.9, 28.6, 29.3, 29.5, 29.6 (7×CH_2), 31.9, 125.7, 129.3, 129.5, 137.2, 141.1, 170.9; IR ($CHCl_3$) ν_{max} 1707, 1516, 1394 cm^{-1}. Anal. Calcd for $C_{39}H_{65}NO_2$: C, 80.77; H, 11.30; N, 2.42. Found: C, 80.81; H, 11.42; N, 2.37.

4.8. 2-Methylene-*N*-*p*-tolyl-succinamic acid (10)

To a stirred solution of itaconic anhydride (2.00 g, 17.8 mmol) in ether (10 mL) at room temperature was added a solution of *p*-toluidine (1.90 g, 17.8 mmol) in ether (10 mL) in a dropwise fashion over a period of 10 min. The reaction mixture was stirred at room temperature for 50 min. and the precipitated product was filtered, washed with ether (2×10 mL) and dried under vacuum to obtain 2-methylene-*N*-*p*-tolyl-succinamic acid **10** (4.00 g, 98% yield); White solid; mp 188–190 °C (ethyl acetate+ethanol); ^{1}H NMR ($CDCl_3$+DMSO-d_6, 200 MHz) δ 2.20 (s, 3H), 3.28 (s, 2H), 5.69 (s, 1H) 6.21 (s, 1H), 6.98 (d, $J=8$ Hz, 2H), 7.39 (d, $J=8$ Hz, 2H), 9.48 (bs, 1H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 20.7, 39.8, 119.3, 127.8, 129.4, 132.2, 136.2, 137.1, 168.0, 168.6; IR (Nujol) ν_{max} 3292, 2700–2500, 1676, 1655, 1630, 1462 cm^{-1}. Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.62; H, 6.05; N, 6.24.

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