

Synthesis of pyran derivatives via three component reaction of isocyanides

Narges Ghasemi^{*a}, and Reza Akbari^b

^aNational Petrochemical Company (NPC), petrochemical Research and Technology Company, Arak Center, Iran

^bDepartment of Chemistry, Faculty of Science, Gonbad Kavous University, P.O.Box 163, Gonbad, Iran.

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Abstract: The reaction between alkyl(aryl) isocyanides and dibenzoylacetylene in the presence of ethyl bromopyruvate leads to ethyl 3,4-dibenzoyl-2-bromomethyl-5-alkyl(aryl)imino-2,5-dihydro-pyran-2-carboxylates in high yields in N-formylmorpholine as solvent. Dialkyl acetylenedicarboxylates react with *tert*-butyl isocyanide and ethyl bromopyruvate to produce 3,4-dialkyl 2-ethyl 2-bromomethyl-5-*tert*-butylimino-2,5-dihydro-pyran-2,3,4-tricarboxylates.

Keywords: Isocyanide, Ethyl bromopyruvate, Dibenzoylacetylene, Three-component reaction, Acetylenic ester.

Introduction

The hexagonal heterocyclic compounds including oxygen such as pyrans are a significant class of compounds having biological properties and exist in natural and synthetic products. Also these compounds play an essential and interest role in bioorganic chemistry [1-2]. The pyrans and fused pyrans have many biological activity such as antimicrobial [3], antifungal[4], antitumor [5], anticoagulant, diuretic, spasmolytic and antianaphylactic.¹¹⁻¹⁵ Furthermore, pyran nucleus exist in some of the natural compounds [6, 7]. Because of the importance of these compounds, some procedures have been investigated for the preparation of pyran derivatives [8-13]. Isocyanides are the only class of stable organic compounds with a formally divalent carbon.

Owing to its reactivity the isocyanide group differs fundamentally from other functional groups [14-17]. One of the classic themes in the chemistry of isocyanides is heterocyclic synthesis [18]. Multi-component reactions (MCRs), by virtue of their convergence, facile execution, and generally high yields of products, have attracted much attention from the point of combinatorial chemistry. Of pivotal importance in this area are the isocyanide-based MCRs such as the versatile Ugi and Passerini reactions [14-19]. The reactivity of nucleophilic carbenes such as isocyanides towards dimethyl acetylenedicarboxylate (DMAD) is well recognized [20-21]. The initially formed zwitterionic intermediate, from DMAD and isocyanide, has been shown to undergo further reaction with different electrophilic reagents, leading to a variety of complex heterocyclic compounds. These reactions have

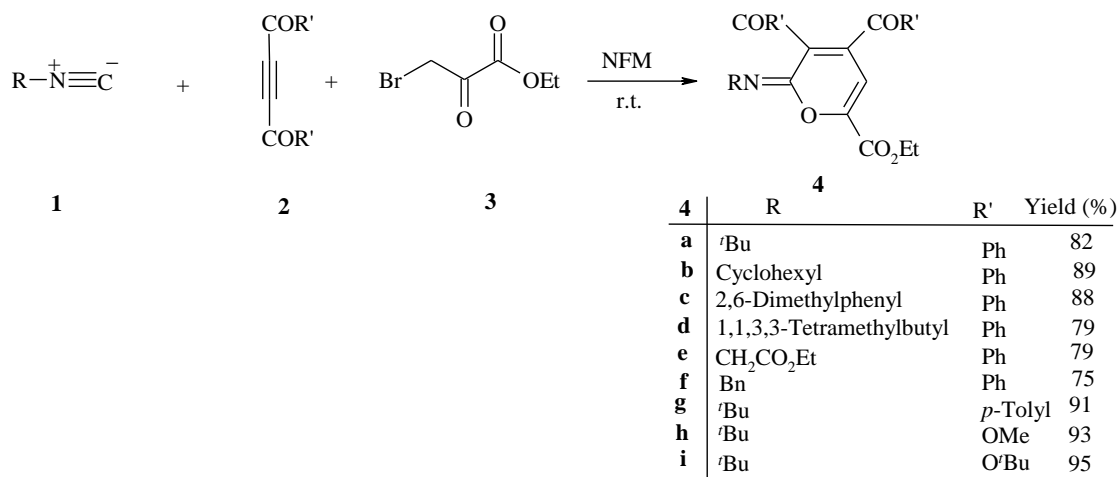
*Corresponding author: Tel: 0098-8633677201-9; Fax: 0098-8633677203, E-mail: naghasemi.16@gmail.com

been the subject of detailed investigation by a number of research groups [22-23]. The reaction of alkyl(aryl) isocyanides and activated acetylenes in the presence of ethyl bromopyruvate was investigated and the results are presented here.

Result and Discussion

tert-Butyl isocyanide (**1a**) and dibenzoylacetylene (**2a**) undergo a smooth reaction in the presence of ethyl bromopyruvate (**3**), in dry diethyl ether at room

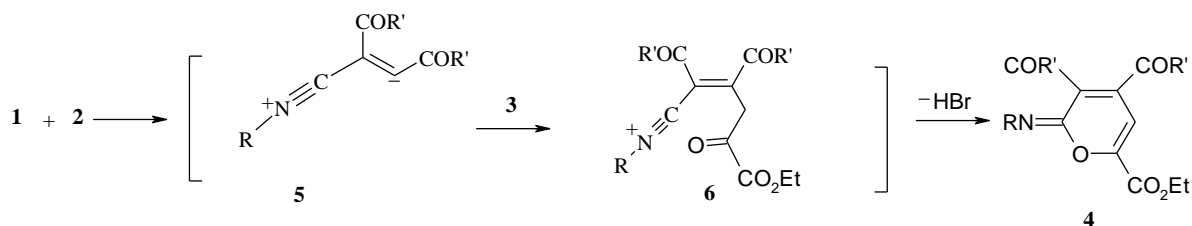
temperature to produce pyran derivative (**4a**) in 82% yield (Scheme 1). Using the isocyanides **1b-1f**, compounds **4b-4i** are obtained in 75-89% yields (see Scheme 1). The structures of compounds **4a-4i** were deduced from their elemental analyses and their IR, ^1H and ^{13}C NMR spectra. The mass spectra of these compounds displayed molecular ion peaks at the appropriate m/z values.



Scheme 1: Synthesis of pyran derivatives in the presence of NFM

The ^1H NMR spectrum of **4a** in CDCl_3 showed a triplet at $\delta = 1.26$ ($^3J_{\text{HH}} = 7.2$ Hz) for the methyl group and a singlet at 1.27 ppm for the *tert*-butyl group. The methylene protons of CH_2Br and OCH_2 moieties are diastereotopic and showed characteristic AB quartet systems at $\delta = 4.18$ and 4.32 ppm. Three single resonances at $\delta = 165.9$, 188.7, and 190.4 ppm are observed in the ^{13}C NMR spectrum of **4a**, which are attributed to the carbonyl groups. The ^1H and ^{13}C NMR spectra of **4b-4i** are similar to those for **4a** except for the imino moieties and the substituents in positions 3 and 4, which show characteristic resonances in appropriate regions of the spectrum.

Mechanistically, it is conceivable that the reaction involves the initial formation of a 1,3-dipolar intermediate **5** between isocyanide and the acetylenic compound [24], which reacts with ethyl bromopyruvate to produce **6**. Cyclization of this zwitterionic intermediate leads to the 2-bromomethyl-5-alkyl(aryl)imino-2,5-dihydro-pyran derivative **4** (Scheme 2).



Scheme 2: Proposed mechanism for the synthesis of **4**

Conclusion

In conclusion, this method is simple and efficient to obtain pyran derivatives. The presented one-pot reaction carries the advantage that not only is the reaction performed under neutral conditions, but the substances can be mixed without any prior activation or modification.

Experimental

1,4-Diaryl-but-2-yne-1,4-diones were prepared by a known procedure [25, 26]. Other chemicals used in this work were purchased from Fluka and used without further purification. Melting points were measured on an Electrothermal 9100 apparatus. NMR spectra were recorded with a Bruker DRX-500 AVANCE instrument (500.1 MHz for ^1H and 125.7 MHz for ^{13}C) with CDCl_3 as solvent. Chemical shifts are given in ppm (δ) relative to internal TMS, and coupling constant (J) are reported in Hertz (Hz). Elemental analyses for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer. These results agreed favorably with the calculated values. Mass spectra were recorded with a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were measured with a Shimadzu IR-460 spectrometer.

General procedure

To a stirred solution of dibenzoylacetylene (0.23 g, 1 mmol) and bromopyruvate (0.19 g, 1 mmol) in 10 mL dry ether was added *tert*-butyl isocyanide (0.12 mL, 1 mmol) at room temperature. The reaction mixture was then stirred for 24 h. The solvent was removed under reduced pressure and the viscous residue was purified by column chromatography on silica gel (Merck 230-400 mesh) using *n*-hexane-EtOAc (3:1) as eluent.

Ethyl 3,4-dibenzoyl-2-bromomethyl-5-*tert*-butylimino-2,5-dihydro-pyran-2-carboxylate (4a)

Pale yellow crystals, yield: 0.42 g (82%), m.p. 115-117 °C. IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 1726, 1680, and 1652 (C=O), 1583 (C=N), 1263 (C-O) cm^{-1} . ^1H NMR: δ = 7.63 (2 H, d, $^3J_{\text{HH}} = 7.6$ Hz, 2 CH_{ortho}), 7.54 (2 H, d, $^3J_{\text{HH}} = 7.5$ Hz, 2 CH_{ortho}), 7.47 (1 H, t, $^3J_{\text{HH}} = 7.3$ Hz, CH_{para}), 7.41 (1 H, t, $^3J_{\text{HH}} = 7.2$ Hz, CH_{para}), 7.25 (2 H, t, $^3J_{\text{HH}} = 7.8$ Hz, 2 CH_{meta}), 7.14 (2 H, t, $^3J_{\text{HH}} = 7.7$ Hz, 2 CH_{meta}), 4.32 (2 H, ABX₃ system, OCH_2), 4.18 (2 H, AB system, $^2J_{\text{AB}} = 11.4$ Hz, $\Delta\nu_{\text{AB}} = 13.2$ Hz, CH_2Br), 1.27 (9 H, s, CMe_3), 1.26 (3 H, t, $^3J_{\text{HH}} = 7.2$ Hz, CH_3) ppm.

^{13}C NMR: δ = 190.4 (C=O), 188.7 (C=O), 165.9 (C=O), 153.0 (C=N), 146.2 (C), 141.7 (C), 136.5 (C_{ipso}), 136.4 (C_{ipso}), 134.0 (CH), 133.9 (CH), 129.2 (2 CH), 129.0 (2 CH), 128.7 (2 CH), 128.4 (2 CH), 89.9 (C), 63.1 (OCH_2), 55.3 (C-N), 33.7 (CH_2Br), 29.6 (CMe_3), 14.0 (CH_3) ppm. MS: m/z (%) = 512 (M^+ , 11), 510 (12), 432 (18), 302 (28), 204 (56), 105 (100), 93 (42), 77 (71), 57 (63).

Anal. Calcd for $\text{C}_{26}\text{H}_{26}\text{BrNO}_5$ (512.4): C, 60.95; H, 5.11; N, 2.73%. Found: C, 61.13; H, 5.15; N, 2.76%.

Ethyl 3,4-dibenzoyl-2-bromomethyl-5-cyclohexylimino-2,5-dihydro-pyran-2-carboxylate (4b)

Pale yellow powder, yield: 0.48 g (89%), m.p. 127-129 °C. IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 1740, 1681, and 1658 (C=O), 1587 (C=N), 1254 (C-O) cm^{-1} . ^1H NMR: δ = 7.63 (2 H, d, $^3J_{\text{HH}} = 7.4$ Hz, 2 CH_{ortho}), 7.52 (2 H, d, $^3J_{\text{HH}} = 7.5$ Hz, 2 CH_{ortho}), 7.44 (1 H, t, $^3J_{\text{HH}} = 7.3$ Hz, CH_{para}), 7.39 (1 H, t, $^3J_{\text{HH}} = 7.2$ Hz, CH_{para}), 7.30 (2 H, t, $^3J_{\text{HH}} = 7.5$ Hz, 2 CH_{meta}), 7.16 (2 H, t, $^3J_{\text{HH}} = 7.2$ Hz, 2 CH_{meta}), 4.33 (2 H, ABX₃ system, OCH_2), 4.22 (2 H, AB system, $^2J_{\text{AB}} = 11.8$ Hz, $\Delta\nu_{\text{AB}} = 19.3$ Hz, CH_2Br), 3.79 (1 H, m, N-CH), 1.84 (2 H, m, CH_2), 1.66 (2 H, m, CH_2), 1.47 (2 H, m, CH_2), 1.40 (2 H, m, CH_2), 1.34 (2 H, m, CH_2), 1.26 (3 H, t, $^3J_{\text{HH}} = 7.2$ Hz, CH_3) ppm.

^{13}C NMR: δ = 190.4 (C=O), 188.5 (C=O), 165.9 (C=O), 155.2 (C=N), 146.9 (C), 140.6 (C), 136.5 (C_{ipso}), 136.4 (C_{ipso}), 134.0 (CH), 133.9 (CH), 129.2 (2 CH), 129.1 (2 CH), 128.4 (2 CH), 128.3 (2 CH), 89.5 (C), 63.6 (OCH_2), 56.9 (C-N), 33.8 (CH_2Br), 33.5 (CH_2), 33.3 (CH_2), 25.5 (CH_2), 24.5 (CH_2), 24.3 (CH_2), 13.9 (CH_3) ppm. MS: m/z (%) = 538 (M^+ , 21), 537 (22), 458 (12), 353 (28), 167 (56), 105 (100), 97 (42), 83 (32), 77 (56). Anal. Calcd for $\text{C}_{28}\text{H}_{28}\text{BrNO}_5$ (538.4): C, 62.46; H, 5.24; N, 2.60%. Found: C, 62.28; H, 5.29; N, 2.65%.

Ethyl 3,4-dibenzoyl-2-bromomethyl-5-(2,6-dimethylphenylimino)-2,5-dihydro-pyran-2-carboxylate (4c)

Orange powder, yield: 0.49 g (88%), m.p. 110-112 °C. IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 1743, 1695, and 1664 (C=O), 1586 (C=N), 1249 (C-O) cm^{-1} . ^1H NMR: δ = 7.66 (2 H, d, $^3J_{\text{HH}} = 7.4$ Hz, 2 CH_{ortho}), 7.51 (2 H, d, $^3J_{\text{HH}} = 7.3$ Hz, 2 CH_{ortho}), 7.46 (1 H, dd, $^3J_{\text{HH}} = 7.5$ Hz, CH_{para}), 7.37 (1 H, t, $^3J_{\text{HH}} = 7.4$ Hz, CH_{para}), 7.33 (2 H, t, $^3J_{\text{HH}} = 7.1$ Hz, 2 CH_{meta}), 7.23 (2 H, t, $^3J_{\text{HH}} = 7.4$ Hz, 2 CH_{meta}), 7.16 (1 H, d, $^3J_{\text{HH}} = 7.4$ Hz, CH of Aryl), 7.11 (1 H, d, $^3J_{\text{HH}} = 7.0$ Hz, CH of Aryl), 7.04 (1 H, t, $^3J_{\text{HH}} = 7.1$ Hz, CH of Aryl), 4.35 (2 H, ABX₃ system, OCH_2), 4.08 (2

H, AB system, ${}^2J_{AB} = 12.4$ Hz, $\Delta\nu_{AB} = 23.1$ Hz, CH₂Br), 2.22 (3 H, s, CH₃), 2.21 (3 H, s, CH₃), 1.35 (3 H, t, ${}^3J_{HH} = 7.2$ Hz, CH₃) ppm. ${}^{13}\text{C}$ NMR: $\delta = 189.8$ (C=O), 188.1 (C=O), 165.3 (C=O), 155.9 (C=N), 149.1 (C), 143.9 (C-N), 140.1(C), 136.1 (C_{ipso}), 136.0 (C_{ipso}), 134.4 (CH), 134.3 (CH), 129.4 (2 CH), 129.3 (2 CH), 128.4 (2 CH), 128.4 (2 CH of Aryl), 127.5 (2 CH), 127.3 (2 C of Aryl), 123.8 (CH of Aryl), 90.5 (C), 63.5 (OCH₂), 32.4 (CH₂Br), 18.4 (CH₃), 18.3 (CH₃), 13.8 (CH₃) ppm. MS: m/z (%) = 560 (M⁺, 18), 558 (17), 480 (31), 302 (28), 106 (25), 120 (20), 105 (100), 77 (48), 57 (45). Anal. Calcd for C₃₀H₂₆ BrNO₅ (560.4): C, 64.29; H, 4.68; N, 2.50%. Found: C, 64.53; H, 4.62; N, 2.53%.

Ethyl 3,4-dibenzoyl-2-bromomethyl-5-(1,1,3,3-tetramethyl-butylimino)-2,5-dihydro-pyran-2-carboxylate (4d):

Pale yellow powder, yield: 0.45 g (79%), m.p. 120-122 °C. IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1735, 1684, and 1631 (C=O), 1587 (C=N), 1281 (C-O) cm^{-1} .

${}^1\text{H}$ NMR: $\delta = 7.62$ (2 H, d, ${}^3J_{HH} = 7.7$ Hz, 2 CH_{ortho}), 7.50 (2 H, d, ${}^3J_{HH} = 7.6$ Hz, 2 CH_{ortho}), 7.44 (1 H, t, ${}^3J_{HH} = 7.3$ Hz, CH_{para}), 7.39 (1 H, t, ${}^3J_{HH} = 7.4$ Hz, CH_{para}), 7.24 (2 H, t, ${}^3J_{HH} = 7.9$ Hz, 2 CH_{meta}), 7.16 (2 H, t, ${}^3J_{HH} = 7.8$ Hz, 2 CH_{meta}), 4.32 (2 H, ABX₃ system, OCH₂), 4.17 (2 H, AB system, ${}^2J_{AB} = 12.7$ Hz, $\Delta\nu_{AB} = 17.5$ Hz, CH₂Br), 1.83 (2 H, s, CH₂), 1.56 (3 H, s, CH₃), 1.55 (3 H, s, CH₃), 1.24 (3 H, t, ${}^3J_{HH} = 7.2$ Hz, CH₃), 1.03 (9 H, s, CMe₃) ppm. ${}^{13}\text{C}$ NMR: $\delta = 190.4$ (C=O), 188.8 (C=O), 166.1 (C=O), 151.8 (C=N), 145.6 (C), 142.3 (C), 136.4 (C_{ipso}), 136.3 (C_{ipso}), 133.9 (CH), 133.8 (CH), 129.2 (2 CH), 129.1 (2 CH), 128.3 (2 CH), 128.1 (2 CH), 89.9 (C), 63.0 (C-N), 58.9 (OCH₂), 55.0 (CH₂), 33.6 (CH₂Br), 31.9 (CH₃), 31.6 (CMe₃), 29.8 (CH₃), 29.7 (C), 13.9 (CH₃) ppm. MS: m/z (%) = 568 (M⁺, 10), 566 (10), 488 (28), 329 (36), 105 (100), 77 (58), 57 (72). Anal. Calcd for C₃₀H₃₄ BrNO₅ (568.5): C, 63.38; H, 6.03; N, 2.46%. Found: C, 63.51; H, 6.06; N, 2.48%.

Ethyl 3,4-dibenzoyl-2-bromomethyl-5-ethoxycarbonylmethylimino-2,5-dihydro-pyran-2-carboxylate (4e):

Pale yellow powder, yield: 0.43 g (79%), m.p. 114-116 °C (dec.). IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1782, 1739, 1697, and 1661 (C=O), 1508 (C=N), 1262 (C-O) cm^{-1} . ${}^1\text{H}$ NMR: $\delta = 7.63$ (2 H, d, ${}^3J_{HH} = 7.5$ Hz, 2 CH_{ortho}), 7.52 (2 H, d, ${}^3J_{HH} = 7.8$ Hz, 2 CH_{ortho}), 7.47 (1 H, t, ${}^3J_{HH} = 7.3$ Hz, CH_{para}), 7.42 (1 H, t, ${}^3J_{HH} = 7.2$ Hz, CH_{para}), 7.26 (2 H, t, ${}^3J_{HH} = 7.4$ Hz, 2 CH_{meta}), 7.16 (2 H, t, ${}^3J_{HH}$

= 7.1 Hz, 2 CH_{meta}), 4.28 (2 H, ABX₃ system, OCH₂), 4.25 (2 H, ABX₃ system, OCH₂), 4.20 (2 H, AB system, ${}^2J_{AB} = 13.1$ Hz, $\Delta\nu_{AB} = 11.4$ Hz, CH₂), 4.12 (2 H, AB system, ${}^2J_{AB} = 12.2$ Hz, $\Delta\nu_{AB} = 18.2$ Hz, CH₂Br), 1.30 (3 H, t, ${}^3J_{HH} = 7.2$ Hz, CH₃), 1.23 (3 H, t, ${}^3J_{HH} = 7.2$ Hz, CH₃) ppm. ${}^{13}\text{C}$ NMR: $\delta = 189.1$ (C=O), 187.8 (C=O), 165.2 (C=O), 164.1 (C=O), 156.5 (C=N), 148.6 (C), 136.2 (C_{ipso}), 136.1 (C_{ipso}), 134.8 (CH), 134.6 (CH), 128.8 (2 CH), 128.7 (2 CH), 128.5 (2 CH), 128.1 (2 CH), 86.8 (C), 64.1 (OCH₂), 63.6 (OCH₂), 50.3 (CH₂-N), 33.1 (CH₂Br), 14.1 (CH₃), 13.9 (CH₃) ppm. MS: m/z (%) = 542 (M⁺, 15), 540 (14), 462 (31), 441 (36), 357 (56), 105 (100), 101 (54), 77 (58), 45 (72). Anal. Calcd for C₂₆H₂₄ BrNO₅ (542.4): C, 57.58; H, 4.46; N, 2.58%. Found: C, 57.79; H, 4.48; N, 2.61%.

Ethyl 3,4-dibenzoyl-2-bromomethyl-5-benzylimino-2,5-dihydro-pyran-2-carboxylate (4f):

Pale yellow crystals, yield: 0.41 g (75%), m.p. 125-127 °C (dec.). IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1754, 1689 and 1655 (C=O), 1585 (C=N), 1269 (C-O) cm^{-1} . ${}^1\text{H}$ NMR: $\delta = 7.64$ (2 H, d, ${}^3J_{HH} = 7.6$ Hz, 2 CH_{ortho}), 7.53 (2 H, d, ${}^3J_{HH} = 7.4$ Hz, 2 CH_{ortho}), 7.45 (1 H, t, ${}^3J_{HH} = 7.4$ Hz, CH_{para}), 7.41 (2 H, t, ${}^3J_{HH} = 7.7$ Hz, 2 CH_{para}), 7.31 (2 H, t, ${}^3J_{HH} = 7.2$ Hz, 2 CH_{ortho}), 7.25 (3 H, t, ${}^3J_{HH} = 7.8$ Hz, 3 CH_{meta}), 7.14 (3 H, t, ${}^3J_{HH} = 7.7$ Hz, 2 CH_{meta}), 4.71 (2 H, AB system, ${}^2J_{AB} = 15.6$ Hz, $\Delta\nu_{AB} = 22.2$ Hz, CH₂Ph), 4.34 (2 H, ABX₃ system, OCH₂), 4.20 (2 H, AB system, ${}^2J_{AB} = 12.7$ Hz, $\Delta\nu_{AB} = 21.2$ Hz, CH₂Br), 1.24 (3 H, t, ${}^3J_{HH} = 7.2$ Hz, CH₃) ppm. ${}^{13}\text{C}$ NMR: $\delta = 190.1$ (C=O), 188.2 (C=O), 165.5 (C=O), 157.7 (C=N), 147.7 (C), 140.1(C), 139.3 (C_{ipso}), 136.3 (C_{ipso}), 136.2 (C_{ipso}), 134.1 (CH), 134.0 (CH), 129.2 (2 CH), 129.1 (2 CH), 128.5(2 CH), 128.4 (2 CH), 128.2 (2 CH), 127.6 (2 CH), 126.6 (CH), 90.2 (C), 63.4 (OCH₂), 51.9 (CH₂), 33.4 (CH₂Br), 13.9 (CH₃) ppm. MS: m/z (%) = 546 (M⁺, 12), 544 (13), 365 (19), 361 (20), 255 (24), 105 (100), 91 (95), 77 (65), 57 (45).

Anal. Calcd for C₂₉H₂₄ BrNO₅ (546.4): C, 63.75; H, 4.43; N, 2.56%. Found: C, 63.96; H, 4.46; N, 2.58%.

Ethyl 2-bromomethyl-5-tert-butylimino-3,4-bis(4-methyl-benzoyl)-2,5-dihydro-pyran-2-carboxylate (4g):

Yellow crystals, yield: 0.49 g (91%), m.p. 123-125 °C (dec.). IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1735, 1675, and 1655 (C=O), 1582 (C=N), 1260 (C-O) cm^{-1} . ${}^1\text{H}$ NMR: $\delta = 8.16$ (2 H, d, ${}^3J_{HH} = 7.6$ Hz, 2 CH of Ar), 8.09 (2 H, d, ${}^3J_{HH} = 7.5$ Hz, 2 CH of Ar), 7.94 (2 H, d, ${}^3J_{HH} = 7.6$ Hz, CH of Ar), 7.63 (2 H, d, ${}^3J_{HH} = 7.5$ Hz, CH of Ar), 4.30

(2 H, ABX₃ system, OCH₂), 4.21 (2 H, AB system, ²J_{AB} = 11.9 Hz, Δv_{AB} = 18.0 Hz, CH₂Br), 2.37 (3 H, s, Me), 2.35 (3 H, s, Me), 1.25 (9 H, s, CMe₃), 1.16 (3 H, t, ³J_{HH} = 7.2 Hz, CH₃) ppm. ¹³C NMR: δ = 193.5 (C=O), 191.8 (C=O), 167.3 (C=O), 155.2 (C=N), 144.7 (C), 143.7 (C), 143.6 (C_{ipso}), 140.6 (C_{ipso}), 136.9 (C_{ipso}), 135.1 (C_{ipso}), 130.7 (2 CH), 130.4 (2 CH), 129.6 (2 CH), 128.6 (2 CH), 85.2 (C), 60.8 (OCH₂), 57.2 (C-N), 34.8 (CH₂Br), 30.6 (CMe₃), 21.7 (CH₃), 21.5 (CH₃), 14.3 (CH₃) ppm. MS: m/z (%) = 540 (M⁺, 20), 538 (19), 511 (17), 495 (27), 460 (19), 420 (42), 300 (28), 120 (100), 93 (42), 77 (36), 57 (64). Anal. Calcd for C₂₈H₃₀BrNO₅ (540.5): C, 62.23; H, 5.59; N, 2.59%. Found: C, 62.46; H, 5.61; N, 2.62%.

2-Ethyl 3,4-dimethyl 2-bromomethyl-5-tert-butylimino-2,5-dihydro-pyran-2,3,4-tricarboxylate (4h):

Pale yellow powder, yield: 0.39 g (93%), m.p. 98-100 °C. IR (KBr) (v_{max}/cm⁻¹): 1726, 1715 and 1710 (C=O), 1553 (C=N), 1260 (C-O) cm⁻¹. ¹H NMR: δ = 4.36 (2 H, ABX₃ system, OCH₂), 4.28 (2 H, AB system, ²J_{AB} = 15.3 Hz, Δv_{AB} = 20.2 Hz, CH₂Br), 3.99 (3 H, s, OMe), 3.90 (3 H, s, OMe), 1.32 (9 H, s, CMe₃), 1.28 (3 H, t, ³J_{HH} = 7.1 Hz, CH₃) ppm. ¹³C NMR: δ = 166.1 (C=O), 164.7 (C=O), 163.7 (C=O), 146.2 (C=N), 146.0 (C), 141.3 (C), 88.2 (C), 62.9 (OCH₂), 55.3 (C-N), 53.1 (OMe), 53.0 (OMe), 33.5 (CH₂Br), 29.9 (CMe₃), 14.2 (CH₃) ppm. MS: m/z (%) = 420 (M⁺, 16), 418 (15), 405 (19), 391 (20), 361 (45), 340 (15), 300 (17), 288 (29), 93 (40), 77 (18), 57 (100). Anal. Calcd for C₁₆H₂₂BrNO₇ (420.3): C, 45.73; H, 5.28; N, 3.33%. Found: C, 45.71; H, 5.30; N, 3.37%.

3,4-Di-tert-butyl 2-ethyl 2-bromomethyl-5-tert-butylimino-2,5-dihydro-pyran-2,3,4-tricarboxylate (4i):

Pale yellow crystals, yield: 0.48 g (95%), m.p. 112-114 °C. IR (KBr) (v_{max}/cm⁻¹): 1724, 1714 and 1710 (C=O), 1549 (C=N), 1269 (C-O) cm⁻¹. ¹H NMR: δ = 4.41 (2 H, ABX₃ system, OCH₂), 4.29 (2 H, AB system, ²J_{AB} = 14.3 Hz, Δv_{AB} = 22.1 Hz, CH₂Br), 1.74 (9 H, s, CMe₃), 1.71 (9 H, s, CMe₃), 1.66 (9 H, s, CMe₃), 1.26 (3 H, t, ³J_{HH} = 7.2 Hz, CH₃) ppm. ¹³C NMR: δ = 165.0 (C=O), 163.8 (C=O), 163.5 (C=O), 153.0 (C=N), 146.0 (C), 142.5 (C), 89.0 (C), 84.0 (CMe₃), 83.4 (CMe₃), 62.1 (OCH₂), 54.3 (C-N), 33.2 (CH₂Br), 29.2 (CMe₃), 28.4 (CMe₃), 28.3 (CMe₃), 13.9 (CH₃) ppm. MS: m/z (%) = 504 (M⁺, 13), 502 (12), 459 (18), 391 (29), 302 (72), 210 (54), 300 (17), 77 (21),

57 (100). Anal. Calcd for C₂₂H₃₄BrNO₇ (504.4): C, 52.39; H, 6.79; N, 2.78%. Found: C, 52.62; H, 6.82; N, 2.81%.

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